



# Information-Gathering Report

*Hospice Quality Reporting Program – Option Year 1*



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## Table of Acronyms

<b>CMS</b>	Centers for Medicare & Medicaid Services
<b>COPD</b>	Chronic Obstructive Pulmonary Disease
<b>CPOT</b>	Critical Care Pain Observation Tool
<b>EORTC-QLQ-C30</b>	European Organization for Research and Treatment of Cancer-Quality of Life Questionnaire-C30
<b>ESAS</b>	Edmonton Symptom Assessment Scale
<b>FACT-G</b>	Functional Assessment of Cancer Therapy: General
<b>HHA</b>	Home Health Agencies
<b>HIS</b>	Hospice Item Set
<b>HOPE</b>	Hospice Outcomes & Patient Evaluation
<b>HQRP</b>	Hospice Quality Reporting Program
<b>IPOS</b>	Integrated Palliative Care Outcomes Scale
<b>IRF</b>	Inpatient Rehabilitation Facilities
<b>LTCH</b>	Long Term Acute Care Hospitals
<b>MIDOS</b>	Minimal Documentation System
<b>MMF</b>	Meaningful Measures Framework
<b>MWM Project</b>	Measuring What Matters Project
<b>NCQA</b>	National Committee for Quality Assurance
<b>NHPCO</b>	National Hospice and Palliative Care Organization
<b>NQF</b>	National Quality Forum
<b>OMH</b>	CMS Office of Minority Health
<b>OY1</b>	Option Year 1
<b>POS</b>	Palliative Care Outcomes Scale
<b>RDOS</b>	Respiratory Distress Observation Scale
<b>SDOH</b>	Social Determinants of Health
<b>SME</b>	Subject Matter Expert
<b>SM-EOLD</b>	Symptom Management at the End-of-Life in Dementia
<b>SNF</b>	Skilled Nursing Facilities
<b>SPADE</b>	Standardized Patient Assessment Data Elements
<b>SWC-EOLD</b>	Satisfaction with Care at the End-of-Life in Dementia
<b>TEP</b>	Technical Expert Panel

## Executive Summary

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### **Background**

Many Americans rely on hospice care for end-of-life support. The Centers for Medicare & Medicaid Services (CMS) pays for hospice services for more than one million Americans each year. These services are critical to a seriously-ill patient population. CMS strives to define, measure, and incentivize high-quality hospice care, including expanding the Hospice Quality Reporting Program (HQRP) over the next several years to include additional meaningful quality measures. To support this work, the Abt team is developing both a patient assessment instrument, known as the Hospice Outcomes & Patient Evaluation (HOPE), and quality measures to describe the quality of care provided to hospice patients. HOPE is expected to replace the current Hospice Item Set (HIS) data-collection tool.

This work began with a review of the existing literature and related resources to inform HOPE development and related quality measures. This information is captured in the [Base Year Information Gathering Report](#). Since that report was released, Abt staff have conducted an in-person Technical Expert Panel (TEP) meeting and held expert interviews to discuss concepts for new HQRP quality measures and how HOPE can support data collection for those measures. These discussions identified areas where additional information was needed to support the expansion of the HQRP. Specifically, in this report we focus on:

- Understanding, through literature reviews and expert interviews, how the Integrated Palliative Outcome Scale (IPOS) can be adapted and used in the HOPE assessment;
- Reviewing updated literature to determine whether HOPE sufficiently captures signs and symptoms of actively dying patients;
- Conducting literature reviews and discussions with hospice pain management experts to inform a quality measure construct for pain management;
- Completing literature reviews to inform a quality measure construct for dyspnea management; and
- Identifying preliminary considerations related to social determinants of health.

### **Integrated Palliative Outcome Scale (IPOS)**

The IPOS, a scale that measures symptoms in patients receiving palliative care, is a compelling scale for use in hospice because it assesses symptom *impact* instead of *severity*. In addition, testing has found adequate reliability and validity for proxy reporters. To further explore using IPOS in the HQRP, we conducted a literature review for evidence supporting using IPOS with hospice patients. We also conducted interviews with IPOS developers to understand how best to integrate IPOS into HOPE. IPOS was developed to assess comprehensive physical and emotional symptoms, information needs, and family-related concerns. Both patient report and proxy report (e.g., clinician or family caregiver proxies) are supported, allowing IPOS use at multiple assessment time points, including when a patient no longer has the capacity to provide their own responses. After discussion with IPOS experts Drs. Irene Higginson (developer of IPOS) and Mevhibe Hocaoglu (IPOS development team member), we have adapted selected IPOS items for HOPE in the areas of symptom impact, anxiety, feeling depressed, and feeling at peace.

### **Actively Dying Patients**

For the signs and symptoms of actively dying, we reviewed a 2013 systematic literature review conducted by Kehl and Kowalkowski that focused on the published signs and symptoms of actively dying patients. We also looked at research assessing the prognostic significance of signs or symptoms for those with

expected survival of one week or less. This was first done as part of the Base Year Information Gathering Report work, and that literature review was repeated in the spring of 2020 to identify any recent publications addressing the following questions: 1) What are the most common signs and symptoms experienced by persons in the last days of life?; and 2) What signs and symptoms predict active death? We added a focus on nursing-science literature for this updated review. Our results confirmed evidence that the following signs and symptoms are present among persons who are actively dying: Cheyne-stokes respiration, apnea, pulselessness of radial artery, peripheral cyanosis, decreased urine output, death rattle, respiration with mandibular movement, non-reactive pupils, decreased response to verbal stimuli, drooping of nasolabial fold, low oxygen saturation, new dysphagia of liquids, and decrease in blood pressure. Our review did not support the use of additional indicators of imminent death.

### ***Information Related to a Clinical Quality Outcome Measure for Pain***

The current HIS includes process measures for pain screening (NQF# 1634) and assessment (NQF# 1637). The pain screening process measure assesses whether patients are screened for pain and whether pain severity is assessed using a standardized tool. The pain assessment measure reports whether patients who screened positive for pain received a comprehensive pain assessment. A pain outcome measure could provide a more comprehensive understanding of the patient experience, for example by focusing on whether hospices provide dying patients with their desired level of pain control. Our fall 2019 TEP provided input on a pain measure construct and articulated several key points for consideration when developing a pain measure, including potential measurement challenges associated with neuropathic pain.

Neuropathic pain is specific type of pain that develops when the nervous system is damaged due to disease or injury. It requires medication be administered more slowly and over more days than medication used for other types of pain. To inform development of a pain quality measure that takes neuropathic pain into consideration, we conducted a literature review to better understand neuropathic pain prevalence and treatments, particularly in a hospice setting, and convened a small technical expert workgroup. The varied causes, manifestations, and diagnostic criteria for neuropathic pain make it difficult to determine its overall impact on patients' health status and quality of life. Our literature review on neuropathic pain epidemiology identified a range in prevalence in the general population, and variability in how it is diagnosed. We found apparent consensus in terms of recommendations for the pharmacological management of neuropathic pain. However, we could not definitively determine whether these recommendations apply in a hospice setting. In addition to this literature review, Abt held a small workgroup with a subset of TEP members that focused on a pain quality measure concept, the results of which will be provided in the 2020 TEP report.

Based on these initial findings, the TEP should continue to discuss refinements to the pain outcome measure concept and how data can be collected to support the measure. Specifically, additional areas to refine include: accounting for changes in pain type and severity; distinguishing between intermittent pain and ongoing pain; determining whether pain will be assessed as a "snapshot" of the patient or use a lookback period; handling patients who refuse to be assessed; and deciding how a measure would apply to different settings of care, among others. We will continue these conversations with the TEP in the fall of 2020 to determine where best to focus our next information gathering activities.

### ***Information Related to a Clinical Quality Outcome Measure for Dyspnea***

Shortness of breath, or dyspnea, is a frequent concern among hospice patients, and its prevalence varies with terminal diagnosis. The goal of quality hospice care is that patients, in particular those who are actively dying, do not experience distress due to persistent shortness of breath at rest. CMS is interested in transitioning the HQRP from reliance on the current process measures related to dyspnea treatment, to an outcome measure that assesses how well hospices manage dyspnea among their patients. Abt's prior work included conducting expert interviews and a literature review to better understand the existing instruments, tools, and scales for assessing the presence and impact of dyspnea in a hospice setting, and to support the importance of dyspnea as a quality measure concept. Additional discussion on dyspnea during

the fall 2019 TEP identified several challenges in developing a dyspnea outcome measure. In particular, TEP participants noted that dyspnea may be one of the most distressing conditions for the patient's caregiver and/or family members to witness. Additionally, the TEP raised the concern that a dyspnea measure may have unintended consequences, such as unnecessary treatment that may exacerbate the patient's symptoms. Furthermore, it can be difficult to treat dyspnea without sufficient training, as effective dyspnea treatment can vary depending on the cause. To help address these concerns, Abt conducted a literature review to gather information on dyspnea prevalence, the relationship between dyspnea and anxiety, the inclusion of patient preferences and goals in a dyspnea quality measure, and the level of inter-rater reliability between existing dyspnea symptom assessment instruments.

Dyspnea prevalence in a hospice and palliative care population varies widely within and between common conditions such as cancer, chronic obstructive pulmonary disease (COPD), heart failure, interstitial lung disease, and dementia. The literature review identified more than 40 available instruments and methods for assessing dyspnea presence and severity, including symptom assessment tools, symptom distress scales, symptom prevalence indicators, and qualitative interviews with patients. Some instruments are diagnosis-specific and have been found to be sensitive to meaningful clinical changes in dementia patients. Several alternatives exist for patients who are unable to self-report.

Anxiety is widely experienced by patients with dyspnea, with anxiety being both a common psychological response to dyspnea and also a predictor or cause of dyspnea. Patients report that gaining control of their thoughts can mitigate anxiety by reducing their perception of both the dyspnea and the anxiety. For example, interventions focused on symptoms of anxiety, such as reassuring the patient that an episode of breathlessness is temporary, can reduce feelings of panic.

The acceptability of and patient preferences for certain dyspnea treatment options (e.g., inhaled or orally administered opioids, breathlessness education, and using hand-held fans) is important to consider when managing dyspnea, as preferences can vary by patient, culture, and diagnosis. Several studies have demonstrated the benefits of individualized dyspnea interventions that allow for patient autonomy and psychological interventions, with negative dyspnea experiences described as those where the patient's autonomy is infringed upon or where needs go unmet. Patients and caregivers can have varying perceptions of dyspnea and its impact. Despite these potential discrepancies, caregiver reports of patient distress can provide valuable information about the care received and whether or not patient needs were met.

Additional work is needed to further inform the development of a quality measure that adequately and appropriately addresses management of dyspnea at end of life. We will further discuss the dyspnea measure concept with the TEP in the fall of 2020, and gather additional information as needed to support development of a dyspnea measure.

### ***Considering Social Determinants of Health***

Social determinants of health (SDOH) include a myriad of nonmedical factors — such as the conditions in which people are born, live, work, and age— that influence health and wellness. The CMS Office of Minority Health (OMH) recommended that, starting in 2019, some SDOH data elements be collected on standardized patient assessment instruments used in long term acute care hospitals (LTCH), inpatient rehabilitation facilities (IRF), skilled nursing facilities (SNF) and home health agencies (HHA). According to the National Quality Forum's 2006 Consensus Report, "A National Framework and Preferred Practices for Palliative and Hospice Care Quality," acknowledging non-medical health factors, respecting patients' unique backgrounds and needs, and committing to equity should be embedded in the general principles of hospice care.

Due to their nuance and intersection, social determinants are difficult to isolate and operationalize. Nevertheless, there are common non-medical variables that may influence individual hospice experience.

For example, women are more likely to have their pain dismissed than men, and pharmacies local to black hospice patients may be less likely to stock adequate pain medication. Recognizing the impact of nonmedical factors on patients' health-related beliefs and behaviors, CMS is implementing standard patient assessments data elements that collect SDOH data in post-acute care settings. The draft HOPE currently includes items for gender identity, sex assigned at birth, sexual orientation, race, ethnicity, and preferred language and need for an interpreter.

### ***Conclusion***

High-quality hospice care honors patient, family, and caregiver needs by addressing physical, psychosocial, emotional, and spiritual well-being throughout the dying experience. To measure high-quality hospice care, the HQRP is working toward developing quality measures that focus on patient outcomes, rather than patient care processes. To that end, Abt has conducted literature reviews and interviews with subject matters experts, based on direction provided by CMS and the TEP convened in November of 2019. We have identified evidence that supports using adapted IPOS items in HOPE to better capture symptom impact on a patient's daily life rather than merely symptom severity. Our updated review of the signs and symptoms of actively dying confirms that our list remains current with the research literature. We have also identified information to support developing quality outcome measures in two key hospice care areas: pain and dyspnea. Our work on both of these measure concepts will be shared with the TEP, which will convene in the fall of 2020, to facilitate progress towards developing outcome measures for HQRP use. We also confirmed that social determinants of health are relevant to hospice care and should be considered in measure development and quality reporting.

## Background and Significance

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Many Americans rely on hospice care for end-of-life support. The Centers for Medicare & Medicaid Services (CMS) pays a per diem for hospice services for more than one million Americans each year.<sup>3</sup> These services are critical to a seriously-ill patient population. CMS continually strives to improve hospice quality and the experience of care for beneficiaries within the context of the Meaningful Measures Framework (MMF)<sup>4</sup>, which prioritizes high-impact quality measure areas that are meaningful to patients, their families and caregivers. CMS seeks to define, measure, and incentivize high-quality hospice care.

CMS anticipates expanding the Hospice Quality Reporting Program (HQRP) over the next several years to include additional meaningful quality measures. The Abt team, under contract to CMS, supports this work. Currently, we are developing a patient assessment instrument, the Hospice Outcomes & Patient Evaluation tool (HOPE), and clinical quality measures to assess the quality of care provided to hospice patients. HOPE is expected to replace the current Hospice Item Set (HIS) data collection tool. The primary goals for HOPE are to reflect the care needs of people through the dying process, prioritize the safety and comfort of individuals enrolled in hospice nationwide, and promote person-centered care that prioritizes psychosocial, spiritual, and emotional support.

The [Base Year Information Gathering Report](#) supported this effort by reviewing available resources to inform HOPE development and related quality measures. That report presented methods and findings from base year information-gathering activities, which included: diverse stakeholder input, review of existing clinical practice guidelines, review of legislation and regulations and their impact on measurement, literature reviews, and a gap analysis of existing instruments and measures.

Since that report was released, Abt conducted an in-person Technical Expert Panel (TEP) to discuss concepts for new HQRP quality measures and how HOPE can support data collection for those measures. These discussions identified areas where additional information was needed to support the expansion of the HQRP. To that end, this Option Year 1 information gathering report focuses on:

- Information for advancing HOPE development:
  - Understanding through literature reviews and expert interviews how the Integrated Palliative Outcome Scale (IPOS) can be adapted or used in HOPE, and
  - Reviewing updated literature to determine whether HOPE is sufficiently capturing signs and symptoms of actively-dying patients.
- Information for outcome measure development:
  - Conducting literature reviews and conversations with experts to inform a quality measure construct for pain management, and
  - Conducting literature reviews to inform a quality measure construct for dyspnea management.

Additionally, we present preliminary information on key social determinants of health for consideration in quality measure development. We will share this report with the TEP prior to their meeting in the fall of 2020 to facilitate continued progress in developing HQRP outcome measures, and refining HOPE to support those measures.

## Integrated Palliative Outcome Scale (IPOS)

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### Background

During HOPE development, we evaluated existing valid and reliable assessment questions and tools to consider what might be used or adapted for HOPE. One such tool was IPOS. Unlike most existing tools, IPOS focuses on symptom impact rather than symptom severity. To thoroughly understand whether IPOS items could be integrated in HOPE, we conducted a literature review focused on IPOS validity and reliability and its usefulness as a symptom assessment tool from both the provider and patient perspectives.

IPOS is a brief patient outcome assessment scale based on the Palliative Outcomes Scales (POS) and POS-symptoms list (POS-S) (“POS-S Generic Patient Card”, 2020). The IPOS is meant to capture the impact of symptoms, needs, concerns, and general status of palliative care patients at all stages of illness, including hospice. IPOS can be used for clinical assessment or to evaluate the quality of care patients are receiving (Murtagh et al., 2019). It has been translated, used, and evaluated as a patient outcome assessment scale in England (Murtagh et al., 2019), Germany (Murtagh et al., 2019), Switzerland (Sterie et al., 2019), Sweden (Lind, 2019), New Zealand (Sandham et al., 2019), and Japan (Sakurai et al., 2019).

Most tools used in the hospice setting, such as the Edmonton Symptom Assessment Scale (ESAS) and Functional Assessment of Cancer Therapy: General (FACT-G), are symptom severity scales. The European Organization for Research and Treatment of Cancer-Quality of Life Questionnaire-C30 (EORTC-QLQ-C30) assesses global quality of life. The IPOS combines elements of those scales and asks how much the patient has been affected by the symptom, resulting in a more comprehensive assessment. To further explore the use of IPOS in the HQR, we conducted both a literature review to find evidence supporting this use of IPOS, and conducted interviews with technical experts to understand how to integrate IPOS into HOPE.

### Evidence supporting IPOS use

#### Literature Review

We conducted a literature review that was limited to the last five years, per CMS direction. We used the MEDLINE/PubMed® database, and supplemented that database with searches in *Google Scholar*. Our search terms included the following: “Integrated Palliative Outcome Scale,” “IPOS,” “integrated palliative care outcome scale,” “hospice” “symptom assessment,” “outcome assessment.” The results addressed questions regarding IPOS validity and reliability, patient and provider perspectives on using IPOS, and identified advantages and disadvantages.

#### Validity and Reliability

A number of studies have evaluated IPOS validity and reliability in eliciting palliative care patients’ experiences of physical symptoms (pain, shortness of breath, weakness, nausea, vomiting, poor appetite, constipation, sore mouth, drowsiness, poor mobility); psychological symptoms (anxiety, depression); family and friends’ status (family anxiety, sharing feelings); spirituality (feeling at peace); and other items (Sakurai et al., 2019). Researchers have used Rasch<sup>1</sup> modeling (Murtagh et al., 2019; Sandham et al., 2019) to demonstrate that the IPOS has internal reliability, consistency, and structural validity for patients receiving hospice care.

Rasch analysis of the IPOS has shown scale consistency across different age and ethnic groups. The IPOS has also shown unidimensionality and consistent interval measurement units along scale responses. Further, when the IPOS is administered for patients or for staff-proxies, it can be used to identify patients who experience higher symptom burden (Murtagh et al., 2019; Sandham et al., 2019). IPOS scores have shown strong to mild correlations relative to scores that used other symptom scales: ESAS  $r=0.68$ ,  $p<0.001$ ; FACT-G  $r=0.66$ ,  $p<0.001$ ; EORTC-QLQ-C30  $r=0.34$ ,  $p<0.001$ ) (Murtagh et al., 2018).

While further research is warranted to confirm interrater reliability for hospice family members using IPOS, Thomas et al.’s 2018 study indicates that IPOS can be initiated with patients who are able to self-report and later, as patients experience decreased cognition, can be used by a proxy to continue assessing concerns identified as important at the end

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<sup>1</sup> A Rasch model is a psychometric tool that shows whether a measure works well for different demographic groups, independent of differing characteristics by evaluating outcome measures properties (Sandham et al., 2019; Sprauge et al., 2018). This model is also able to identify biases that may be pertinent to items or questions on the scale and the appropriate randomly determined order of items to ensure reliability and validity.

of life. Thomas assessed interrater reliability for IPOS in hospice patients along with a family or staff member. Proxy respondents had fair to moderate agreement with the patient, depending on the item ( $\kappa = 0.2 - 0.6$ ). Staff were more likely to provide lower ratings than patients, whereas family members' responses were more often in agreement with patient responses ( $\kappa = 0.6$ ). Therefore, when patients are unable to complete IPOS, family members may be more accurate proxies than healthcare providers.

### ***Patient and Provider Perspectives***

Patients have reported that IPOS promotes self-care and enables discussions and reflections on their physical and emotional well-being. Patients have also reported that IPOS helped them describe the real impacts of their illnesses to their healthcare providers (Högberg et al., 2019). One challenge that patients reported is occasional difficulty choosing IPOS scores that best describe symptom impact when their symptoms are fluctuating. This corresponds to findings in studies of other patient outcome assessment scales that capture symptom severity, such as the ESAS, a commonly used symptom subscale (Schildmann et al., 2016).

According to Lind et al. (2019), healthcare providers have reported that IPOS is a simple scale comprising easy-to-understand questions, with content that was not perceived to be distressing to their patients. Providers noted that, when they had sufficient training in IPOS, using it could increase and improve communication with patients and made these conversations more substantive. Generally, providers reported that the IPOS structure facilitated accurately documenting the patient's condition without adversely affecting providers' workflow. Lind et al. (2019) also reported that providers expressed concern that patients' symptom assessment by proxies when patients were unable to self-report was subjective. They often chose not to use IPOS for such patients. Lind's study team further reported that clinician education on using IPOS and ongoing support were key factors to implementation success.

### ***Advantages and disadvantages***

Through the literature review, we identified many advantages to adapting or using IPOS items in HOPE, with few disadvantages. These are described in **Table 1**.

**Table 1: Advantages and Disadvantages of using IPOS items in HOPE**

Advantages	Disadvantages
<ul style="list-style-type: none"> <li>• Although 28 percent of hospice patients are admitted in the last seven days of life (NHPCO, 2018), a significant number are likely able to and prefer to report their symptom experiences and preferences to their care teams.</li> <li>• IPOS items are appropriate for the hospice population because they can be asked of patients able to self-report and then later asked of caregivers familiar with those patients, when death appears imminent or when self-report is no longer possible.</li> <li>• Patients have reported that the IPOS promotes self-care and reflections on their physical and emotional well-being and enables discussions with providers.</li> <li>• Healthcare providers have reported that the IPOS is a simple scale comprising easy-to-understand questions, with content that was not perceived to be distressing to their patients.</li> <li>• The IPOS uniquely assess the impact of physical, psychological, and spiritual symptoms on daily life, going beyond other scales that measure symptoms only in terms of severity.</li> <li>• Rasch analysis of the IPOS has shown scale consistency across population groups, indicating that different groups can be assessed equally for comparison purposes.</li> <li>• The IPOS has shown unidimensionality and consistent interval measurement units along scale responses, indicating that the scale is able to accurately measure palliative and hospice care preferences and outcomes.</li> </ul>	<ul style="list-style-type: none"> <li>• More testing is needed to confirm interrater reliability for IPOS proxy versions. Initial testing demonstrated that family proxies more closely reflected patient responses than staff proxies.</li> <li>• Providers have expressed concern that the IPOS assessment of patients' symptoms completed by proxy, when patients were unable to self-report, was subjective and therefore often chose not to use the IPOS for such patients.</li> <li>• Since Lind's study team (2019) reported that clinician education on IPOS and ongoing support were key factors in implementation success, provider education and ongoing support is critical for hospice IPOS use.</li> </ul>

## Modifying IPOS items for HOPE

In August 2019, the Abt team met with [Professor Irene Higginson](#), the IPOS developer and the Head of Department, Head of Division, and Director of the Cicely Saunders Institute at King’s College London, to discuss ways in which IPOS might be modified for inclusion in HOPE. After this initial meeting, the Abt team adapted certain IPOS items and conducted focus group sessions, cognitive testing, and pilot testing. Subsequently on April 21, 2020, the Abt team met with Dr. Higginson and [Dr. Mevhibe Hocaoglu](#) to discuss recommendations for further modifying IPOS items for HOPE. We also discussed Abt’s proposed acknowledgment for using modified IPOS items. **Table 2** provides the selected IPOS items, the corresponding first modification for HOPE, and the feedback received.

**Table 2: IPOS item, corresponding modified HOPE item, and feedback received**

Symptom Impact Item	
IPOS Item	Question #2: Please tick one box that best describes how the patient has been affected by each of the following symptoms over the past 3 days
HOPE Item	Question #10: Select the patient’s worst symptom severity in the past day for each symptom using the symptom severity responses below.
Feedback	<ul style="list-style-type: none"> <li>• Dr. Higginson questioned use of the term “severity,” noting that clinician and patient interpretation may be of the level of symptom intensity, which is not what was intended by the Abt team.</li> <li>• If “severity” is retained, the response option “none” is potentially confusing, as severity implies a relative symptom impact, rather than the presence or absence of the symptom.</li> <li>• Dr. Higginson noted the difference between the original IPOS version of this question, which asks about the symptom impact on a patient (a general question), versus Abt’s version that asks about symptom the severity of the symptom impact on specific activities, such as sleep, day-to-day activities, and interactions with others. Dr. Higginson noted, for example, that patients may experience problems with any of these specific activities, yet still characterize the effect of a symptom on those functions as mild. Drs. Higginson and Hocaoglu suggested that Abt has too much focus on day-to-day activities, and recommend more general wording about symptom impact on the person.</li> <li>• Dr. Higginson identified shortness of breath/dyspnea as the most difficult symptom to appropriately assess in the adapted item set. While it is expected that patients may have dyspnea as they conduct their desired normal activities, the goal is to not reach severe dyspnea where the patient becomes panicked. If they are pacing activities well, patients may have some shortness of breath, but would not reach a situation where they panic and possibly call 911 seeking emergency care.</li> </ul>
Anxiety Items	
IPOS Items	Question #3: Has s/he been feeling anxious or worried about his/her illness or treatment? Question #4: Have any of his/her family or friends been anxious or worried about the patient?
HOPE Items	Question #21: Patient feeling anxious or worried ... about patient’s illness or treatment Question #22: “Family feeling anxious or worried ... about the patient.”
Feedback	<ul style="list-style-type: none"> <li>• Dr. Higginson explained the IPOS utilizes questions that tap into multiple sources of anxiety [which supports the multiple modified HOPE items]. She noted this impacts psychological well-being and quality of life.</li> </ul>
Feeling Depressed Items	
IPOS Item	Question #5: Do you think s/he felt depressed?
HOPE Item	Question #20: Over the past three days . . . How often does the patient seem depressed?
Feedback	<ul style="list-style-type: none"> <li>• Dr. Higginson mentioned that the modified HOPE item is not used alone in IPOS for depression screening, but in conjunction with a second item about peace. She stated that the depression and peace items in IPOS work well together, and will share a paper with the Abt team that describes this.</li> </ul>
Feeling at Peace Items	
IPOS Item	Question #6: Do you think s/he has felt at peace?
HOPE Item	Question #46: How concerned are you with being at peace with your life?
Feedback	<ul style="list-style-type: none"> <li>• Drs. Higginson and Hocaoglu identified this item as the one with which they see the most potential difficulty for accuracy and utility in assessment, regarding the language used in Abt’s adaptation. They consider this a complicated construct with a double meaning (whether the patient is concerned and whether they are at peace included in the same question). They are not sure what the answers to this question would mean. They noted that the item originated in the U.S. with Karen Steinhauer at Duke University, and recommended that the Abt team check that resource for more information on phrasing. Dr. Hocaoglu suggested asking, “Have you been at peace [in the last three days]?”</li> </ul>

Additionally, Dr. Higginson emphasize that for HOPE items that allow patient or proxy (staff or family) assessment/response, comparing responses across time can only be done if the rater is the same across each time point.

The Abt team inquired about any quality measures currently in use (or in development) that are based POS or IPOS items. We were particularly interested in how these measures are specified (i.e., numerator, denominator, exclusions) and how these measures perform. Drs. Higginson and Hocaoglu confirmed that POS/IPOS data are used primarily for internal quality improvement and reports, or scorecards, rather than publicly-reported quality measures. Drs. Higginson and Hocaoglu also confirmed that there are scant published data about internal quality improvement efforts using the POS/IPOS, and will look for examples that could be shared.

Dr. Higginson confirmed Abt's proposed text for acknowledging permission to adapt the IPOS was correct. Specifically, Abt will use the following language: *Adapted with the permission of Irene Higginson, Cicely Saunders Institute, and King's College London as the intellectual-property owners of the IPOS v[insert the version of the appropriate IPOS].*

### **Next Steps**

The IPOS is a compelling scale for use in hospice because it assesses symptom *impact* instead of *severity*, and has adequate reliability and validity for proxy reporters. As such, the HOPE development team has adapted some IPOS items for HOPE use. In hospice, many patients are both able to and prefer to self-report symptoms, feelings, goals, and needs at the time of admission. However, a number of patients only receive hospice care in the last few days of life when they may be unable to self-report. IPOS has been developed to assess comprehensive physical and emotional symptoms, information needs, and family-related concerns. Both patient report and proxy report (e.g., clinician or family caregiver proxies) can be used, allowing the IPOS to be used at multiple assessment time points, including when a patient no longer has the capacity to provide their own responses. We have incorporated the feedback from Drs. Higginson and Hocaoglu into HOPE in preparation for Alpha testing. If additional information is received from Drs. Higginson and Hocaoglu we will review it to determine if and how additional refinements to data collection should be made.

## Actively Dying Patients

### Background

Patients entering hospice while actively dying are an important consideration for designing an HQRP assessment tool. In 2015, 7.7% of Medicare Beneficiaries enrolled in hospice spent three days or less enrolled in hospice services. During our interviews, stakeholders voiced concern that assessments for these patients should collect only the most basic information to avoid unduly burdening the actively dying person and their primary caregivers/family. Examples include moving a patient to check for skin integrity, or asking the caregivers to leave the room while an assessment is done such that they cannot hold vigil. To minimize data collection burden for actively dying patients and their caregivers, HOPE would include skip pattern logic for these patients, so that it collects only the information necessary for the care plan and applicable quality measure calculations. This information-gathering activity seeks to inform HOPE development by understanding the most current literature on the signs and symptoms of actively dying.

In 2019, as part of our Base Year Information Gathering Report, Abt reviewed a systematic literature review conducted by Kehl and Kowalkowski (2013) focused on the published signs and symptoms of actively dying patients. We also looked at research assessing the prognostic significance of signs or symptoms for those with expected survival of one week or less. As part of the Base Year Information Gathering Report work, the Abt team identified 2,274 articles related to defining actively dying, selected 81 articles for review, and incorporated 34 of those articles into the report. From these papers, the Abt team identified prevalent signs and symptoms of actively dying patients. While none of these studies were generalizable to a broad hospice population dying in various care settings, we compiled and reviewed a list of significant prevalent signs and symptoms, and presented it to CMS for review.

In 2020 (Option Year 1), the Abt team updated the Base Year review to identify any recent publications addressing the research questions, with an added focus on nursing-science literature. Consistent with the Base Year Information Gathering Report, search terms included: *imminently dying, terminal phase, active death, actively dying, predictors, prognostic model, variables, signs, symptoms, factors, predicting, death, dying, mortality, survival, imminent death, last week, last 2 days, last 3 days, last week, final week, final 2 days, final 3 days, 48 hours.*

### Signs and Symptoms of actively dying

This literature review was intended to update Abt's Base Year literature review, and focus more closely on the last week of life. Our goal was to address two questions:

- What are the prevalent symptoms or signs in the last days of life?
- What symptoms or signs predict the last days of life?

Thus, the present review searched for papers that attempted to determine the prognostic significance of signs or symptoms with expected survival of one week or less. This review was intended to identify any new literature from our previous literature review on this topic as well as to focus the search on the nursing literature. The following criteria were applied (**Table 3**):

**Table 3: Inclusion & Exclusion Criteria for Literature Review**

Inclusion Criteria	Exclusion Criteria
<ul style="list-style-type: none"><li>• Article published after 2010</li><li>• Sample size 30 and greater</li><li>• Information on <i>prevalence</i> and/or <i>predictions/prognostic value</i> of signs &amp; symptoms of the actively dying</li><li>• Studied within one week of death</li></ul>	<ul style="list-style-type: none"><li>• Children age 18 and younger</li><li>• Retrospective recall by survey respondents</li><li>• Withdrawal of life support studies</li><li>• Articles that reported only laboratory values</li></ul>

In this most recent review we found a number of articles that employed physician or nurse retrospective report and collected this information shortly after patient death. While excluded from our analysis, in line with the criteria set by Kehl and Kowalkowski (2013), we present information on these studies separately. **Table 4** presents the search methods we used to gather articles. We expanded the search methods used by Kehl et al. (2012) to identify articles that reported predictor and/or prognostic models.

**Table 4. Literature Search Methods & Yield**

	BY Search: Replication of Kehl & Kowalkowski (2013)	BY Search: Expansion of Kehl & Kowalkowski (2013) to focus on prediction	OY1 Search
Database	PubMed	PubMed	PubMed, CINAHL, PsychINFO
Search terms and parameters:	(death OR terminal care OR palliative care OR end of life OR dying OR dying process OR hospice OR hospice care) AND (signs OR symptoms OR signs and symptoms OR signs and symptoms respiratory OR signs and symptoms digestive OR neurobehavioral manifestations OR neurologic manifestations OR skin manifestations OR behavioral symptoms OR affective symptoms OR depression) AND full text[ <i>sb</i> ] AND Humans[Mesh] AND English[ <i>lang</i> ] AND adult[MeSH]) year 2000 newer	((predictors OR prognostic model OR variables OR signs OR symptoms OR factors OR signs symptoms OR predicting)) AND (imminently dying OR terminal phase OR death OR dying OR mortality OR survival OR active death OR actively dying OR imminent death)) AND (last week OR last 2 days OR last 3 days OR last week OR final week OR final two days OR final three days OR 48 hours)) AND full text[ <i>sb</i> ] AND Humans[Mesh] AND English[ <i>lang</i> ] AND adult[MeSH]) NOT fetal) NOT infant) NOT pregnant) NOT suicide, year 2000 newer	(predictors OR “prognostic model” OR variables OR signs OR symptoms OR factors OR “signs symptoms” OR “signs and symptoms” OR predicting) AND (“imminently dying” OR “terminal phase” OR death OR dying OR mortality OR survival OR “active death” OR “actively dying” OR “imminent death” OR “end of life” OR “terminal care” OR “dying process”) AND (“last week” OR “last 2 days” OR “last 3 days” OR “last week” OR “final week” OR “final two days” OR “final three days” OR “48 hours”) AND full text[ <i>sb</i> ] AND Humans[Mesh] AND English[ <i>lang</i> ] AND adult[MeSH]) NOT fetal) NOT infant) NOT pregnant) NOT suicide , year 2010 newer
Total Hits:	17,000+ total hits, approximately 10,000 reviewed due to software limitations (sorted by Best Match)	2,274 total hits, all reviewed	1,612 total hits, all reviewed
Selection for Abstract Review:	53 articles	28 articles	104 articles
Selection for Full Review:	20 articles	11 articles	58 articles
Final Selection:	23 total articles included in review + 3 articles from citation tracking + 8 articles from original Kehl review = 34 total articles		20 articles

**Results**

Our systematic literature review found 1,612 articles, of which 58 were identified for review, yielding 20 articles that met all inclusion criteria and were not included in the previous review.

Key descriptive findings from our review include:

**Study type**

- 70 percent of articles (n=14) reported prevalent symptoms related to actively dying
- 30 percent of articles (n=6) reported on the prognostic significance of symptoms or models

**Population**

- 13 studies examined a population with cancer or other primary diseases
- 2 studies examined a cancer-only population
- 1 focused on chronic kidney disease
- 1 focused on heart failure

- 3 did not provide diagnosis information

### *Symptoms studied*

- The signs or symptoms that were most often reported or studied were pain (n=11 studies), dyspnea (n=9), anxiety (n=7), and nausea (n=7).

**Table B1** in **Appendix B** summarizes 14 articles examining signs and symptoms in the last week of life, as well as 6 studies examining the prognostic strength of various models. None of these newly identified studies report on the prognostic significance of signs and symptoms. **Table B2** in **Appendix B** presents the frequency of signs and symptoms studied in our review. This updated literature review confirmed the following signs and symptoms for actively dying<sup>2</sup>:

- Cheyne-stokes respiration
- Apnea
- Pulselessness of radial artery
- Peripheral cyanosis
- Decreased urine output\*
- Death rattle
- Respiration with mandibular movement
- Non-reactive pupils\*
- Decrease response to verbal stimuli
- Drooping of nasolabial fold
- Low oxygen saturation\*
- New dysphagia of liquids
- Decrease in blood pressure\*

**Table B3** in **Appendix B** presents additional literature that, though not strictly consistent with Kehl and Kowalkowski's methodology, nonetheless may be valuable when considering identifying imminent death. These studies also support our initial findings. In sum, we examined the prevalence of signs and symptoms of actively dying (i.e., the last week of life) in these articles, and found them to be consistent with our previous work.

### *Next Steps*

The signs and symptoms listed above were included in both cognitive and pilot testing of HOPE, and our updated literature review provided no evidence that we should consider additional indicators of imminent death.

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<sup>2</sup> Items with \* were not included in the second round of pilot testing.

## Information related to a Clinical Quality Outcome Measure for Pain

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### **Background**

Offering dying patients their desired amount of pain relief is one of the three key pillars of palliative care provided by hospice. Severe pain significantly impacts quality of life for the dying. As such, pain management is an important foundation in quality measurement and reporting.

The current HIS includes a process measure for pain screening (NQF# 1634) and assessment (NQF# 1637). The pain screening process measure assesses whether patients are screened for pain and whether pain severity is assessed using a standardized tool. The pain assessment measure reports whether patients who screened positive for pain received a comprehensive pain assessment. An outcome measure for pain could focus, for example, on whether hospices provide dying patients with their desired level of pain control. Our fall 2019 TEP provided input on a pain measure construct based on HOPE items.

### **Pain Management as an Outcome Measure**

The TEP discussion articulated several key points for consideration when developing a pain measure. Two areas of further analysis and research were identified to support refinement efforts:

- Review the evidence base and determine the desired outcome or outcome(s) for pain measurement: pain crisis management, reduction of patient pain, or alignment to patient/caregiver preferences.
- Refine pain treatment measurement, including potential adjustments for specific types of pain, such as neuropathic or patient preferences for pain (i.e., a patient preference to tolerate some pain in order to avoid unwanted medication side effects).

Neuropathic pain is a specific pain type that develops when the nervous system is damaged due to disease or injury. Though noting any pain impacting the patient should be addressed, several clinicians on the TEP suggested that including neuropathic pain in an outcome measure would be difficult. Specifically, neuropathic pain is a unique type of pain that requires medication be administered more slowly and over more days than medication used for other types of pain.

TEP members and CMS staff agreed that further research on neuropathic pain in hospice, both through a review of published research and primary data collection, such as subject matter expert (SME) interviews, was needed to inform pain outcome measure development. They indicated these activities should 1) address inclusion of neuropathic pain in a pain quality measure, and 2) ensure that HOPE has the items needed to support data collection for such a measure. Other considerations include whether to use a single symptom outcome measure vs. a multi-symptom outcome measure that includes pain, and how to capture patient preferences and goals.

To inform pain quality measure development, we conducted a literature review to better understand the neuropathic pain prevalence and treatment, particularly in a hospice setting, and convened a small technical expert workgroup to discuss pain measure development considerations.

### **Addressing neuropathic pain**

#### **Literature Review**

Abt conducted a limited literature review on neuropathic pain in the context of hospice. Using the MEDLINE/PubMed database, we focused on recent literature (published within the last five years) that satisfied the search criteria listed below. Abt also conducted a supplementary search using Google Scholar. Search terms included: *neuropathic pain, nerve pain, neurogenic pain, neuralgia, hospice care, hospice and palliative care nursing, palliative medicine, palliative care, hospice, hospice care*. Additional details on this literature review are available in **Appendix C**.

#### **Prevalence of Neuropathic Pain**

The varied causes, manifestations, and diagnostic criteria for neuropathic pain make it difficult to determine its overall impact on patients' health status and quality of life. A comprehensive literature review on neuropathic pain epidemiology identified a range in prevalence in the general population — a discrepancy likely attributable to a “lack of consensus on a definition, diagnostic criteria, and appropriate and consistent use of screening tools” (van Hecke, 2013). Van Hecke et al. (2013) estimated neuropathic pain prevalence in the general population to be 6.9% to 10%, with Mathieson et al., (2015) citing that in patients attending pain clinics it can be as high as 52 percent.

Meanwhile, some patient populations, such as those with cancer, are disproportionately affected by neuropathic pain. A survey conducted in 50 palliative care centers in Italy suggested that more than one in three patients with cancer pain also experienced neuropathic pain, as determined by their physician (Roberto et al., 2016). In an observational study by Harada, et al. (2016), the prevalence of neuropathic pain in cancer patients was just over 23 percent. Because pain intensity is typically higher among patients in advanced stages of cancer than those in the early stages, there is a specific need for research about neuropathic pain diagnosis and treatment among those receiving end-of-life care (Harada et al., 2016).

### ***Clinical Treatment of Neuropathic Pain***

Clinical practice guidelines are intended to “facilitate more consistent, effective, and efficient medical practice” (Deng et al., 2016). Despite some scientists’ concern about the varied understanding of and response to neuropathic pain (van Hecke et al., 2013), Deng and colleagues (2016) assert in their recent systematic review that clinical practice guidelines for neuropathic pain are fairly consistent regarding diagnosis, assessment, and pharmacological management. The Canadian Pain Society’s consensus statement on the pharmacological management of neuropathic pain is consistent with Deng et al.’s treatment recommendations, including a four-tiered approach to pharmacological management (Mu et al., 2017). Although neuropathic pain duration and severity depend largely on the underlying condition, pharmacological treatment is typically effective for symptom palliation (Ballantyne et al., 2010).

Despite apparent “consistency” in recommendations for the pharmacological management of neuropathic pain, “data from other populations cannot necessarily be extrapolated into hospice/palliative care practice” (Sanderson et al., 2014). In a study conducted by Sanderson and colleagues (2014), only 9 percent of hospice patients benefited from gabapentin (a first-line agent) “without also experiencing any harm.” While it is difficult to separate the direct negative side effects of treatment from the expected physical (and often cognitive) deterioration among hospice patients, this study nevertheless highlights the unique considerations around pain treatment for hospice patients, as well as the need for controlled studies (as opposed to cohort studies) to determine the clinical benefits and harms of pharmacological treatment for this population.

### ***Technical Expert Panel Workgroup***

In the spring of 2020, Abt held a small workgroup with a subset of TEP members focused on a pain quality measure concept. Abt convened the workgroup three times to provide additional input on developing an outcome measure for pain. The workgroup again reiterated the importance of patient preferences in determining acceptable outcomes for pain, and understanding the impact of pain on the patient given the wide variability in the tolerance of pain among patients. Full results from this work group will be provided in the 2020 TEP report.

### ***Next Steps***

Thus far, we have reviewed neuropathic pain’s definition, prevalence, treatment, and screening methods. Prevalence varies, and effective treatments for the hospice population is unclear. Additional areas to refine a pain outcome measure include accounting for changes in pain type and severity, distinguishing between intermittent pain and ongoing pain, determining whether pain will be assessed as a patient “snapshot” or use a lookback period, handling patients who refuse to be assessed, and deciding how a measure would apply to different care settings, among others. We will continue these conversations with the TEP in the fall of 2020 to determine where best to focus our next information gathering activities.

## Information related to a Clinical Quality Outcome Measure for Dyspnea

### Background

Shortness of breath, or dyspnea, is a frequent concern among hospice patients, and its prevalence varies depending on their terminal illness. Two out of three people experience dyspnea with diagnoses such as cancer with lung involvement, chronic obstructive pulmonary disease (COPD), heart failure, and dementia (Kamal et al., 2014). The goal of quality hospice care is that patients, in particular ones who are actively dying, are not experiencing distress with persistent shortness of breath at rest.

The HQRP wants to transition from the current dyspnea measures, which assess dyspnea treatment, to an outcome measure that instead assesses how well hospices manage dyspnea among their patients. The Base Year Information Gathering activities related to dyspnea included conducting expert interviews and a literature review to better understand the existing instruments, tools, or scales for assessing the presence and impact of dyspnea in hospice, and to support the importance of dyspnea as a quality measure concept.

The TEP discussed dyspnea further in the fall of 2019 and identified several challenges in developing a dyspnea outcome measure. In particular they noted that dyspnea may be one of the most distressing conditions for the patient's caregiver and/or family members and raised concerns that the measure may have unintended consequences, such as unnecessary treatment that may exacerbate the patient's symptoms. Furthermore, it can be difficult to adequately treat dyspnea without sufficient training, as effective treatment can vary by cause. To help address these concerns, we conducted a literature review to gather information on the following key questions:

- What is dyspnea prevalence by condition (for hospice and terminal palliative populations)?
- What is the relationship between dyspnea and anxiety, and how might this inform a hospice quality measure?
- How can we account for patient preferences and goals related to dyspnea in hospice quality measure?
- What is the level of interrater reliability between existing symptom assessment instruments?

### Literature review methods and results

Our search terms for the Option Year 1 (OY1) literature review included: *palliative care, end of life, hospice care, terminally ill, terminal care, assessment tool(s), surveys and questionnaires, questionnaire(s), self-report, instrument(s), scale(s), instrumentation, psychometric(s), inter-rater reliability, anxiety, prevalence, cancer, COPD, congestive heart failure, heart failure, and pneumonia*. Note these terms vary somewhat from the Base Year Information Gathering Report, which was intended as an update to the 2017 Agency for Healthcare Quality (AHRQ) technical brief "Assessment Tools for Palliative Care" (Aslakson et al., 2017). For this review, we limited results to publications in the last ten years, and restricted our review to source literature in most cases by excluding systematic literature reviews. Our literature review found 768 articles, of which 291 were identified for review, yielding 72 articles that met all inclusion criteria. **Appendix D** provides detailed results of the literature review.

### Primary Diagnoses and Dyspnea

Dyspnea is a common symptom among patients receiving hospice or palliative care. Dyspnea prevalence in this population varies widely within and between the conditions of interest, such as cancer, COPD, heart failure, interstitial lung disease, and dementia. This information is present in **Table 5**. Patients with certain types of cancers, such as lung cancer, experience higher rates of dyspnea than with other cancers, as do patients with a COPD diagnosis. In many cases, dyspnea prevalence increases as death becomes more imminent.

**Table 5: Dyspnea Prevalence by Condition in Patients Receiving Hospice or Palliative Care**

Condition	Dyspnea Prevalence*
Cancer	14% to 97%
<i>Lung cancer</i>	41% to 97%
<i>Advanced soft tissue sarcoma</i>	49%
<i>Other or unspecified cancer</i>	14% to 91%
COPD	55% to 90%
Heart Failure	25%
Interstitial Lung Disease	75% to 91%
Dementia	35% to 60%

\*This table provides a high level summary of prevalence rates by condition, however within a given condition these rates vary based on factors such as when the assessment was performed, or the severity of dyspnea being assessed. More specific information on the prevalence by condition can be found in Table 1 of the Appendix.

Notably, the experience of dyspnea can vary by condition. For example, in one cohort study, dyspnea was correlated with lower satisfaction with hospice care among caregivers of heart failure patients, but not cancer patients. This suggests that hospices may be differentially-equipped to manage dyspnea related to the etiology of certain diagnoses (MacKenzie, 2016).

### *Measuring Dyspnea Severity at End of Life*

In addition to IPOS, discussed above, we identified more than 40 instruments and methods available for assessing dyspnea presence and severity<sup>3</sup>. These include symptom assessment tools, symptom distress scales, symptom prevalence indicators, and qualitative indicators like interviews with patients. The ESAS, a self-reported patient assessment tool that measures symptom severity, is a commonly-used tool. Other valid instruments to measure dyspnea include the London Chest Activities of Daily Living Scale (Reilly, 2017), the Minimal Documentation System (MIDOS) (Simon, 2014), the PERS<sup>2</sup>ON scale (Masel, 2016), and the revised ESAS (ESAS-r) (Kako, 2018). Some instruments are diagnosis-specific, like the Symptom Management at the End-of-Life in Dementia (SM-EOLD) and Satisfaction with Care at the End-of-Life in Dementia (SWC-EOLD) scales (Kiely, 2012), which have been found to be sensitive to meaningful clinical changes in dementia patients.

While patients who are able to communicate their symptoms can use one of the tools noted above, several alternatives exist for patients who are unable to self-report. However multiple studies have shown physician assessments correlate more strongly with instrument-based assessments for dyspnea *presence* than for *severity*. For example, MIDOS-based assessments and physician assessments were found to agree in over 80 percent of cases for dyspnea presence, versus more than 65 percent of cases for dyspnea severity (Simon, 2014). The Respiratory Distress Observation Scale (RDOS) is a reliable tool for measuring dyspnea presence, intensity, and response to treatment for patients unable to self-report (Persichini, 2015; Campbell, 2015; Campbell, 2010). Generally there is a high degree of agreement across instruments, with RDOS having been demonstrated to positively correlate with Dyspnea-NRS and Dyspnea-cat, D-VAS (Zhuang, 2018), and the Critical Care Pain Observation Tool (CPOT) (Reavis, 2018). The RDOS also exhibits strong inter-rater reliability with two trained raters (Zhuang, 2018), but it is a multi-part assessment that may be burdensome if integrated into HOPE.

A number of existing quality measures capture dyspnea management in patients receiving hospice or palliative care. The NQF domain "physical aspects of care" accounts for about one third of quality measures identified in a systemic review of the literature (Kamal, 2014). Dyspnea is addressed in 26 percent of these measures and remains an important quality measurement focus at the end-of-life (Kamal, 2014). This represents significant progress from prior work that identified a limited number of quality measures addressing dyspnea (Mularski, 2010). However, additional work remains. In 2015, the Measuring What Matters (MWM) project released a list of ten candidate quality indicators for hospice and palliative care, two of which capture dyspnea management but are not outcome measures (Dy, 2015). The relevant measures, which are currently in the HQRP, are:

- The Dyspnea Screening and Management indicator quantifies the percentage of patients with advanced chronic or serious life-threatening illnesses who are screened for dyspnea. For those who are diagnosed with moderate or severe dyspnea, a documented plan of care to manage dyspnea is developed.
- The Screening for Physical Symptoms indicator, based on the PEACE dataset, measures the percentage of seriously-ill patients receiving specialty palliative care in an acute hospital setting for more than one day, or patients enrolled in hospice for more than seven days who had a screening for physical symptoms (pain, dyspnea, nausea, and constipation) during the admission visit.

### *Anxiety and Dyspnea*

Anxiety is widely experienced among patients with dyspnea; the symptoms frequently co-occur in patients with one of the diagnoses listed in **Table 5** (Qian, 2018; Chan, 2013; Barata, 2016; Damani, 2019). Dyspnea presence has been found to

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<sup>3</sup> Lists presented in the section are intended to be illustrative rather than exhaustive.

predict anxiety (Zweers, 2018), with an increased predictive power at increased levels of dyspnea severity (Hofmann, 2017). However, anxiety has been identified as both a common psychological response to dyspnea (Janssen, 2015; Schunk, 2019; Mercadante, 2016), and a predictor or cause of dyspnea (Ho, 2012; McKenzie, 2020; Ekström, 2016). For example, anxiety can cause dyspnea through increased respiratory rate and subsequent hyperventilation (Livermore, 2010). Furthermore, anxiety and panic disorders can heighten the perceptions of sensations like dyspnea (Livermore, 2010; Janssen, 2015). Patients report that gaining control of their thoughts can mitigate anxiety, reducing their perception of both dyspnea and anxiety (Bove, 2017). For example, interventions focused on symptoms of anxiety, such as reassuring the patient that an episode of breathlessness is temporary, can reduce feelings of panic (Qian, 2018).

### ***Patient Preferences***

Managing dyspnea is ranked as one of the most important needs by terminally ill older adults (Ben Natan, 2010), though symptom management preferences can vary by patient, culture, and diagnosis group (Dunger, 2015; Simon, 2012; Thongkhamcharoen, 2012). In one study, when patients were asked to use a 10-point scale to indicate “At what level would you feel comfortable with this symptom?” responses ranged from 0 to 6. This highlights the heterogeneity of experiences with dyspnea and personal priorities concerning symptom management (Hui, 2016). The acceptability of and patient preferences for certain treatment options (e.g., inhaled or orally administered opioids, breathlessness education, and using hand-held fans) is important to consider in managing dyspnea (Simon, 2012; Qian, 2018; Ellis, 2012). Because individual patient goals may change over time (Mercadante, 2019), treatment acceptability and preference should be an ongoing conversation.

The side effects of certain interventions may be outweighed by perceived treatment benefits and symptom impact on daily life. Because oxygen is perceived as “lifesaving” or as a “lifeline” by advanced cancer patients, for example, the legitimate disadvantages of oxygen therapy are perceived as relatively minor or non-existent (Jaturapatporn, 2010). Several studies have also demonstrated the benefits of individualized interventions that allow for patient autonomy and psychological interventions on patients experiencing dyspnea (Peng, 2019). Negative experiences with dyspnea care were those where the patient’s autonomy was infringed or where needs went unmet. For example, among patients with advanced COPD, both patients and caregivers perceived that providers were often unaware of the problem posed by symptoms like dyspnea (Schunk, 2019). Conversely, another study found that providers over-estimated the impact of dyspnea on the patient’s quality of life (Khan, 2012).

While both patients and caregivers report that dyspnea has a significant impact on their lives, their perceptions of dyspnea burden can vary significantly (Ferreira, 2020). Caregivers, for example, may be distressed by watching a patient chronically struggling to catch their breath, an experience to which the patient himself or herself has adapted, while the patients finds acute episodes of breathlessness much more distressing (Ferreira, 2020). Despite potential discrepancies between patients’ experiences of dyspnea and caregivers’ assessment of the dyspnea experiences, caregiver reports of patient distress can provide valuable information about the care received and whether or not patient needs were met (Singer, 2016). Indeed, one study found a positive correlation between patients’ and caregivers’ assessments of dyspnea in advanced cancer patients receiving palliative care (Perez-Cruz, 2016).

### ***Next Steps***

Additional work is needed to continue constructing a quality measure that adequately and appropriately addresses dyspnea management at end of life. This review summarized dyspnea prevalence among patients with the conditions identified by the TEP as having a strong evidence base for treatment, and explored patient preferences regarding dyspnea treatment more broadly. However, further work is needed to better understand patient preferences concerning the treatment options specific to those diagnoses of interest. Furthermore, as discussed in this review, watching patients experience shortness of breath can be disconcerting for caregivers. The TEP raised this issue and emphasized the need for a quality measure that takes individual patient preferences into account and is framed in such a way as to not encourage rash decision-making or unnecessary treatment. We will continue these conversations with the TEP in the fall of 2020 to determine where best to focus our next information gathering activities.

## Considering Social Determinants of Health

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### Background

Social determinants of health (SDOH) include a myriad of nonmedical factors — such as the conditions in which people are born, live, work, and age (“Social Determinants”, 2020) — that influence health and wellness. These conditions may be rooted in built environments, like neighborhoods, or in less tangible realms, like economic status, education, or community context (“Social Determinants”, 2020). While the specific social determinant categories vary across scholars and organizations (Richard & Marmot, 2003; “Social Determinants”, 2020), all definitions acknowledge the significant effect of these nonmedical conditions on patients’ health-related knowledge, attitudes, beliefs, and behaviors (Braveman et al., 2011)

The CMS Office of Minority Health (OMH) seeks to reduce health disparities and improve the health of all minority populations — including people with disabilities, rural populations, and racial, ethnic, and sexual minorities — in part through “data collection [that] strengthens our understanding of the relationship between social determinants of health and health care use across diverse populations” (James, 2019). Ultimately, comprehensive patient data collection is required to facilitate better care coordination and to track changes among target populations over time (Office of Minority Health, 2015). OMH recommended that, starting in 2019, some SDOH data elements be collected on standardized patient assessment instruments in several post-acute care provider settings (James, 2019).

To inform this initiative, OMH, with support from the National Committee for Quality Assurance (NCQA), convened a listening session in December 2018 to elicit feedback from stakeholders — including health systems, research groups, government agencies, and advocacy organizations — about measuring social determinants of health (CMS, 2018). Insights from this listening session are reflected in CMS’s proposed specifications for standardized patient assessment data elements (SPADEs) for certain post-acute care settings, such as home health (Center for Clinical Standards and Quality, 2019)

With its holistic care delivery philosophy, hospice is uniquely poised to address social determinants of health. According to the National Quality Forum’s 2006 Consensus Report, “A National Framework and Preferred Practices for Palliative and Hospice Care Quality,” acknowledging non-medical health factors, respecting patients’ unique backgrounds and needs, and committing to equity should be embedded in the general principles of hospice care (National Quality Forum, 2006).

### Results of Brief Literature Review

Due to their nuance and intersection, social determinants are difficult to isolate and operationalize. Nevertheless, there are common non-medical variables that may influence individual hospice experience. For example, women are more likely to have their pain dismissed than men (Sutherland, 2016), and pharmacies local to black hospice patients may be less likely to stock adequate pain medication (Rizzuto, 2018). In addition, the lived experience of different populations influences their preferences. Though the TEP expressed concerns about patients in rural areas facing more challenges than those in urban areas, particularly when considering the dyspnea measure, our review found widespread geographic access to hospice in the United States. The vast majority of the population lives within 30 minutes driving time of a hospice, with an average driving time of 15 minutes between where people live and the nearest hospice (Carlson et al., 2010).

**Appendix E1** contains a detailed summary of literature addressing the effects of race, gender, sexual orientation, religion, culture, and geography on hospice care. Our search terms for the OY1 literature review included: *social determinants of health, health disparities, health equity, health inequity, hospice experience, hospice enrollment, hospice utilization, and end-of-life care*. This brief review used Google Scholar, and was not intended to be comprehensive, but more to provide an initial summary of SDOH considerations in hospice care.

### Next Steps

This work confirms that there are non-medical factors that can affect hospice care quality, and the importance of patient preferences in hospice care. CMS recognizes this in their work to implement SPADEs that collect SDOH data in post-acute care settings. The current HOPE draft includes items such as location, gender, sex, sexual orientation, age, race, language, and resource needs. All of these items can help us better understand the hospice population, and how different characteristics can influence quality of care. As we continue to discuss measure constructs, this research can help inform whether measures can or should be re-specified, risk adjusted, or stratified so as to present the clearest picture of the quality of hospice care.

## Conclusion

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High-quality hospice care honors patient, family, and caregiver needs by addressing physical, psychosocial, emotional, and spiritual well-being throughout the dying experience. It follows that measuring high-quality hospice care must be based on the principles of addressing physical, psychosocial, emotional, and spiritual well-being for patients, their families and caregivers.

To support this work, the HQRP is working toward developing clinical quality measures focused on patient outcomes, rather than the process of assessing and treating patients in hospice. To that end, we have conducted literature reviews and interviews with subject matters experts, as directed by CMS and the TEP that convened in November of 2019. Specifically, we have evidence supporting the integration of IPOS items into HOPE, which will allow greater focus on the impact of symptoms on a patient's daily life rather than symptom severity alone. Our updated review of actively dying signs and symptoms confirm that our work to support these patients and their caregivers remains up-to-date.

We have also provided information to support development of clinical quality outcome measures in two key areas of hospice care: pain and dyspnea. Based on concerns raised by the TEP, we explored neuropathic pain prevalence and treatment. We also explored the primary conditions with which dyspnea occurs, how it is assessed, its relationship with anxiety, and patient and caregiver preferences in dyspnea treatment. We will share our work on both of these measure concepts with the TEP to provide additional information on their expressed areas of concern. We also provide preliminary information on the ways SDOH can be considered when determining hospice care quality. This information will be shared with the TEP so we can collectively continue to make progress towards developing outcome measures for use in the HQRP.

## Appendices

### Appendix A: IPOS Literature Review Tables

Table A1 presents a summary of the articles examined that discuss IPOS.

**Table A1: Summary of IPOS Literature**

Citation	Country	Year	Study Design	Conclusion
Murtagh, F. E., Ramsenthaler, C., Firth, A., Groeneveld, E. I., Lovell, N., Simon, S. T., Denzel, J., Guo, P., Bernhardt, F., Schildmann, E., van Oorschot, B., Hodiamont, F., Streitwieser, S., Higginson, I. J., & Bausewein, C. (2019). A brief, patient- and proxy-reported outcome measure in advanced illness: Validity, reliability and responsiveness of the Integrated Palliative care Outcome Scale (IPOS). <i>Palliative Medicine</i> , 33(8), 1045–1057. <a href="https://doi.org/10.1177/0269216319854264">https://doi.org/10.1177/0269216319854264</a>	UK, Germany	2019	<p>Concurrent, cross-cultural validation study of the Integrated Palliative care Outcome Scale - both (1) patient self-report and (2) staff proxy-report versions. We tested construct validity (factor analysis, known-group comparisons, and correlational analysis), reliability (internal consistency, agreement, and test-retest reliability), and responsiveness (through longitudinal evaluation of change).</p> <p>In all, 376 adults receiving palliative care, and 161 clinicians, from a range of settings in the United Kingdom and Germany.</p>	The Integrated Palliative care Outcome Scale is a valid and reliable outcome measure, both in patient self-report and staff proxy-report versions. It can assess and monitor symptoms and concerns in advanced illness, determine the impact of healthcare interventions, and demonstrate quality of care. This represents a major step forward internationally for palliative care outcome measurement.

Citation	Country	Year	Study Design	Conclusion
The integrated palliative care outcome scale for patients with palliative care needs: factors related to and experiences of the use in acute care settings. (2019). <i>Palliative &amp; Supportive Care</i> . <a href="https://doi.org/10.1017/S1478951518001104">https://doi.org/10.1017/S1478951518001104</a>	Sweden	2019	Data were collected as a part of the evaluation of the feasibility of an implementation strategy for introducing IPOS. Data from three participating acute care units were included. We used descriptive and analytical statistics; a qualitative content analysis was also performed.	Found an association between healthcare professionals' participation in training sessions and patients who completed IPOS, indicating the need for a high degree of attendance at the training to achieve successful implementation. The healthcare professionals expressed feelings of insecurity concerning the use of IPOS indicating a need for further education and clinical support in its use of IPOS. Nevertheless, use of IPOS was considered to contribute to improved care of patients with palliative care needs.
Högberg, C, Alvariza, A, Beck, I. (2019) Patients' experiences of using the Integrated Palliative care Outcome Scale for a person-centered care: A qualitative study in the specialized palliative home-care context. <i>Nurs Inq</i> . 26:e12297. <a href="https://doi.org/10.1111/nin.1229">https://doi.org/10.1111/nin.1229</a>	Sweden	2019	The study adopted a qualitative approach with an interpretive descriptive design. Interviews were performed with 10 patients, of whom a majority were diagnosed with incurable cancer.	The study finds that using IPOS is beneficial and provide ways to enable person-centered care and with advantage could be used in specialized palliative home care. The results may help overcome barriers and facilitate the use of patient-reported outcome measures (PROMs).
Sterie, A.-C., Borasio, G. D., & Bernard, M. (2019). Validation of the French Version of the Integrated Palliative Care Outcome Scale. <i>Journal Of Pain And Symptom Management</i> , 58(5), 886–890.e5. <a href="https://doi.org/10.1016/j.jpainsymman.2019.07.012">https://doi.org/10.1016/j.jpainsymman.2019.07.012</a>	French	2019	The validation took place in 12 palliative care units and mobile teams. At baseline (T1) and three days later (T2), patients' general health status, palliative care needs (IPOS-Fr), and quality of life (McGill Quality of Life Scale-Revised) were assessed by patients and staff.	IPOS-Fr has fair to good validity, especially with regard to interrater agreement and construct validity, is sensitive to positive change, and has good interpretability and acceptability for patients and staff. IPOS-Fr is not optimal in terms of internal consistency and structure when using subscale scores, except for the emotional subscale.

Citation	Country	Year	Study Design	Conclusion
Sandham, M. H., Medvedev, O. N., Hedgecock, E., Higginson, I. J., Siegert, R. J., & Medvedev, O. (2019). A Rasch Analysis of the Integrated Palliative Care Outcome Scale. <i>Journal of Pain &amp; Symptom Management</i> , 57(2), 290–296. <a href="https://doi.org/10.1016/j.jpainsymman.2018.11.019">https://doi.org/10.1016/j.jpainsymman.2018.11.019</a>	New Zealand	2019	Responses of 300 community-dwelling palliative care patients were subjected to Rasch analysis using the partial credit model.	The modified IPOS showed excellent reliability for a clinical measure in assessing the overall palliative care needs of a patient. The provided ordinal-to-interval conversion table accounts for unique contribution of each symptom to the overall symptom burden and easy to use without the need to modify the original IPOS format.
Schildmann, E. K., Groeneveld, E. I., Denzel, J., Brown, A., Bernhardt, F., Bailey, K., Guo, P., Ramsenthaler, C., Lovell, N., Higginson, I. J., Bausewein, C., & Murtagh, F. E. M. (2016). Discovering the hidden benefits of cognitive interviewing in two languages: The first phase of a validation study of the Integrated Palliative care Outcome Scale. <i>Palliative Medicine</i> , 30(6), 599–610. <a href="https://doi.org/10.1177/0269216315608348">https://doi.org/10.1177/0269216315608348</a>	UK, Germany	2016	Bi-national (United Kingdom/Germany) cognitive interview study using ‘think aloud’ and verbal probing techniques. Interviews were audio-recorded, transcribed verbatim and analysed using thematic analysis and pre-defined categories. Results from both countries were collated and discussed. The Integrated Palliative care Outcome Scale was then refined by consensus.  Purposely sampled patients from four palliative care teams in palliative care units, general hospital wards and in the community.	Cognitive interviewing proved valuable to increase face and content validity of the questionnaire. The concurrent approach in two languages – to our knowledge the first such approach in palliative care – benefited the refinement. Psychometric validation of the refined Integrated Palliative care Outcome Scale is now underway.
Thomas, H. L., Clazie, S., Charlett, A., & Amsler, P. (2018). P-62 Comparison of family and staff members’ assessments of hospice inpatients’ symptoms using IPOS. <i>BMJ Supportive &amp; Palliative Care</i> , 8(Suppl 2), A32.		2018	Once a week over one year, for each patient in the inpatient unit who had completed their own IPOS, a family member, doctor, nurse and NSA completed a proxy IPOS. Measured agreement using weighted Kappa statistics.	Whenever possible, patients should be supported to complete their own IPOS, as proxy respondents do not agree strongly with patients. When patients are unable to complete an IPOS, family members are the most appropriate proxy. Under-estimation of issues by staff has implications for our ability to accurately assess and address our patients’ needs. Conversely, over-estimation of issues, particularly the extent to which a patient feels at peace, may lead to under-estimation of quality of life.

Citation	Country	Year	Study Design	Conclusion
Dodds, N. (2018) P-61 How are you? The use of IPOS in clinical assessments. <i>BMJ Supportive &amp; Palliative Care</i> . 8:A32.		2018	Development and adjustment of IPOS tool taken from patients at St Christopher's Hospice	IPOS tool can be used to structure and lead a patient-center holistic assessment. Therefore, with some minor adjustments, to include questions relating to patient wishes and goals, along with a patient information leaflet, to make the tool more 'patient friendly', we now have a variation of the IPOS tool to structure all of our formal clinical assessments in our different care settings.
McLintock, S., Forshaw, C., Marley, K. (2017) P-77 Audit of outcome measure use in a hospice <i>BMJ Supportive &amp; Palliative Care</i> . 7:A37		2017	This is a retrospective audit, aiming to capture all patients in a one month period who were admitted to the IPU or who attended the day hospice for assessment. The standards (all with 100% targets) will include: - iPOS offered to patients on admission or at first assessment -iPOS offered weekly thereafter - Reason for non-compliance documented when iPOS not completed -AKPS and Phase of Illness discussed weekly at the MDT meeting A secondary project will involve documenting baseline scores and changes in scores during admission or time attending the day hospice.	This project encompasses an audit to assess compliance and a secondary project to explore changes in outcome measures during an episode of care. We hope this information will help to further promote the use of outcome measures in clinical practice throughout the hospice.
POS-PAL. (2012) The Palliative care Outcome Scale outline for new & current users. <a href="https://pos-pal.org/maix/pos-and-ipos-summary.php">https://pos-pal.org/maix/pos-and-ipos-summary.php</a>	N/A	N/A	N/A	IPOS is an exciting development, integrating the most important questions from POS, POS-S and the APCA African POS. It has been welcomed by patients and professionals as a more streamlined measure which is brief, yet which still captures their most important concerns - both in relation to symptoms, but also extending to information needs, practical concerns, anxiety or low mood, family anxieties and overall feeling of being at peace.

Citation	Country	Year	Study Design	Conclusion
Bausewein, C., Schildmann, E., Rosenbruch, J., Haberland, B., Tänzler, S., & Ramsenthaler, C. (2018). Starting from scratch: implementing outcome measurement in clinical practice. <i>Ann Palliat Med</i> , 7(S3), S253-S61.	Germany	2018	N/A	The following steps were used to implement routine outcome measurement in clinical care in a university palliative care unit. (I) Selection of outcomes of interest by the clinical leads and head of department: most prevalent symptoms; psychological, practical and spiritual concerns, functional status, carer burden; (II) selection of outcome measures: Integrated Palliative Care Outcome Scale (IPOS), phase of illness, Australian Karnofsky Performance Status; (III) educational component about the measure and how to use results: team meetings and team retreat with introduction of outcome measurement in palliative care, chosen measures and role plays with use of measures; (IV) selection of responsible consultant on the ward as coordinator and facilitator for outcome measurement; (V) who applies the measure and its periodicity. Implementation of outcome measurement in clinical routine is feasible following a structured process.
Sprague, E., Siegert, R. J., Medvedev, O., & Roberts, M. H. (2018). Rasch analysis of the Edmonton symptom assessment system. <i>Journal of pain and symptom management</i> , 55(5), 1356-1363.	New Zealand	2018	ESAS data collected from 229 patients enrolled in a community hospice service were evaluated using a partial credit Rasch model with RUMM2030 software (RUMM Laboratory Pty, Ltd., Duncraig, WA). Where disordered thresholds were discovered, item rescoring was undertaken. Rasch model fit and differential item functioning were evaluated after each iterative phase.	The ESAS satisfied unidimensional Rasch model expectations in a 12-item format after minor modifications. This included uniform rescoring of the disordered response categories and creating super items to improve model fit and clinical utility. The accuracy of the ESAS scores can be improved by using ordinal-to-interval conversion tables published in the article

Citation	Country	Year	Study Design	Conclusion
Nekolaichuk, C., Watanabe, S., & Beaumont, C. (2008). The Edmonton Symptom Assessment System: a 15-year retrospective review of validation studies (1991–2006). <i>Palliative Medicine</i> , 22(2), 111-122.	Canada	2008	Using a comprehensive literature search, the authors identified and screened 87 publications. Thirteen articles were selected for in-depth review, based on the following inclusion criteria: psychometric studies with a primary focus on the ESAS, 1991–2006 publication dates and peer-reviewed English language publications.	The use of varying instrument formats and limited psychometric evidence support the need for further ESAS validation studies, including the involvement of patients.
Hui, D., & Bruera, E. (2017). The Edmonton Symptom Assessment System 25 years later: past, present, and future developments. <i>Journal of pain and symptom management</i> , 53(3), 630-643.	United States	2017	Narrative review.	ESAS has evolved over the past 25 years to become an important symptom assessment instrument in both clinical practice and research. Future efforts are needed to standardize this tool and explore its full potential to support symptom management.
Sakurai, H., Miyashita, M., Imai, K., Miyamoto, S., Otani, H., Oishi, A., ... & Matsushima, E. (2019). Validation of the integrated palliative care outcome scale (IPOS)–Japanese version. <i>Japanese Journal of Clinical Oncology</i> , 49(3), 257-262.	Japan	2019	This is a multicenter, cross-sectional observational study. We assessed the missing values, prevalence, test–retest reliability, criterion validity and known-group validity in Japanese adult cancer patients. Patients provided responses to IPOS, European Organization for Research and Treatment for Cancer Quality of Life Questionnaire-Core 30 (EORTC QLQ-C30), and Functional Assessment of Chronic Illness Therapy- Spiritual 12 (FACIT-Sp12). Our medical staff provided responses to Support Team Assessment Schedule (STAS).	IPOS-Japanese version is a valid and reliable tool. The scale is useful in assessing physical, psychological, social and spiritual symptoms and in measuring outcomes of adult cancer patients in Japan.

Citation	Country	Year	Study Design	Conclusion
Richardson, L. A., & Jones, G. W. (2009). A review of the reliability and validity of the Edmonton Symptom Assessment System. <i>Current Oncology</i> , 16(1), 55.	Canada	2009	A systematic search for articles from 1991 through 2007 found thirty-nine peer-reviewed papers from 25 different institutions, thirty-three of which focused on patients with cancer. Observations, data, and statistics were collated according to relevance, reliability, validity, and responsiveness.	The ESAS is reliable, but it has restricted validity, and its use requires a sound clinical process to help interpret scores and to give them an appropriate level of attention. Research priorities are to further develop the ESAS for assessing a greater number of important physical symptoms (and to target “physical symptom A review of the reliability and validity of the Edmonton Symptom Assessment System L.A. Richardson BSc* and G.W. Jones MSc MD*† distress”), and to develop a similar instrument for emotional symptoms.
National Hospice and Palliative Care Organization (NHPCO) Facts and Figures (2018 Edition)		2018		

## Appendix B: Signs and Symptoms of Actively Dying Literature Review Results

**Table B1** presents a summary of 12 articles examining signs and symptoms in the last week of life, as well as 6 studies examining the prognostic strength of various models. None of these newly-identified studies report on the prognostic significance of signs and symptoms.

**Table B2** presents the frequency of signs and symptoms studied in our review.

**Table B3** presents additional literature that, though not strictly consistent with Kehl's methodology, nonetheless may be valuable when considering identifying imminent death. These studies also support our initial findings.

**Table B1: Summary of Studies Examining Signs and Symptoms in the Last Week of Life**

Citation	Design and data source	Setting and sample	Diagnoses included	Time frame to death	Symptom prevalence	Prognostic significance of symptoms
1. Nagase, M.O. et al. (2012). A retrospective chart review of terminal patients with cancer with agitation and their risk factors	Retrospective chart review	Japan, university hospital N = 126 patients with cancer who died NOTE: Includes patients 16 and older	Cancer	7 days	<ul style="list-style-type: none"> <li>Agitated delirium 49%.</li> <li>Agitated delirium occurred most frequently 6 days before death.</li> </ul>	
2. Axelsson, L.A. et al. (2018). Unmet Palliative Care Needs Among Patients With End-Stage Kidney Disease: A National Registry Study About the Last Week of Life	Registry study based on data from the Swedish Register of Palliative care (SRPC)	Sweden N = 472 patients with chronic kidney disease who died in various settings	Chronic kidney disease	7 days	<ul style="list-style-type: none"> <li>Pain 69%</li> <li>Respiratory secretion 46%</li> <li>Anxiety 41%</li> <li>Confusion 30%</li> <li>Shortness of breath 22%</li> <li>Nausea 17%</li> </ul>	
3. Rajala, K.L. et al. (2016). End-of-life care of patients with idiopathic pulmonary fibrosis	Prospective cohort study with retrospective analysis of health care documentation during the 6 months that preceded death	Finland N = 59 deceased patients with idiopathic pulmonary fibrosis (IPF)	Cardiovascular disease Hypertension Diabetes Atrial fibrillation Obstructive lung disease Cancer	7 days	<ul style="list-style-type: none"> <li>Dyspnea 66%</li> <li>Pain 31%</li> <li>Delirium 19%</li> <li>Anxiety/depression 17%</li> <li>Cough 15%</li> <li>Nausea 7%</li> <li>Constipation 2%</li> </ul>	
4. Öhlén, J.R. et al. (2017) Variations in Care Quality Outcomes of Dying People: Latent Class Analysis of an Adult National Register Population	Cross-sectional retrospective study using data from the Swedish Register of Palliative care (SRPC)	Sweden N = 87,026 decedents with expected deaths in various settings	Neoplasms Circulatory Dementia Respiratory Other	7 days	<ul style="list-style-type: none"> <li>Pressure sores (20.3%)</li> </ul>	

Citation	Design and data source	Setting and sample	Diagnoses included	Time frame to death	Symptom prevalence	Prognostic significance of symptoms
5. Eriksson, H.M. et al. (2016) End of Life Care for Patients Dying of Stroke: A Comparative Registry Study of Stroke and Cancer	Retrospective study using data from the Swedish Register of Palliative care (SRPC)	Sweden, hospitals and nursing homes N = 3,252 patients who had died expectedly of stroke or cancer	Stroke Cancer	7 days	<ul style="list-style-type: none"> <li>Dyspnea (16.3% stroke patients, 23.3% cancer patients)</li> <li>Death rattles ( 60.7% stroke patients, 49.2% cancer patients)</li> <li>Pain (42.7% stroke patients, 78% cancer patients)</li> <li>Anxiety (18.9% stroke patients, 42.3% cancer)</li> <li>Confusion (7.9% stroke patients, 23.6% cancer)</li> <li>Decubitus (14.5% stroke patients, 13.8% cancer)</li> </ul> <p>Compared to the patients with cancer, the patients dying of stroke had:</p> <ul style="list-style-type: none"> <li>Higher Odds Ratio (OR) for having death rattles (OR 1.7;95% CI 1.47–1.96)</li> <li>Lower ORs for registering the symptoms of pain, nausea, confusion, anxiety and dyspnea</li> </ul>	
6. Ekström, M.A. et al. (2016). Breathlessness During the Last Week of Life in Palliative Care: An Australian Prospective, Longitudinal Study	Prospective, longitudinal cohort study using data from the Australian Palliative Care Outcomes Collaboration (PCOC)	Australia, palliative care N = 12,778 patients who had at least one breathlessness measurement during the final seven days of life	Cancer Neurologic disease Cardiovascular disease Respiratory failure Other	7 days	<ul style="list-style-type: none"> <li>Moderate or severe breathlessness 35%</li> </ul> <p>The observed mean breathlessness from the beginning of the last week of life did not change as death approached.</p>	

Citation	Design and data source	Setting and sample	Diagnoses included	Time frame to death	Symptom prevalence	Prognostic significance of symptoms
7. Andersson, S. et al. (2018). Factors Associated With Symptom Relief in End-of-Life Care in Residential Care Homes: A National Register-Based Study	Retrospective study using data from the Swedish Register of Palliative care (SRPC)	Sweden, residential care homes N = 22,855 decedents with expected deaths	Cancer Heart disease Dementia Diabetes Stroke Other neuro disease Lung disease Post-fracture Other disease	7 days	<ul style="list-style-type: none"> <li>• Pain 69%</li> <li>• Anxiety 44%</li> <li>• Shortness of breath 14%</li> <li>• Nausea 10%</li> </ul>	
8. Klint, A. et al. (2019) Dying With Unrelieved Pain- Prescription of Opioids Is Not Enough	Observational cohort study	Sweden  N = 161,762 expected deaths	Cancer Non-cancer	7 days	<ul style="list-style-type: none"> <li>• Pain 68%</li> </ul>	
9. Bailey, F.A. et al. (2012). Opioid pain medication orders and administration in the last days of life	Retrospective chart review	USA, Veterans Administration Medical Centers  N = 1068 patients who died	Cancer Dementia Lung disease Heart disease Kidney disease Liver disease Stroke HIV Acute illness	7 days	<ul style="list-style-type: none"> <li>• Pain 81%</li> </ul>	

Citation	Design and data source	Setting and sample	Diagnoses included	Time frame to death	Symptom prevalence	Prognostic significance of symptoms
10. Brännström, M. et al. (2012) Unequal care for dying patients in Sweden: a comparative registry study of deaths from heart disease and cancer	Retrospective registry study, using the Swedish Palliative Registry	Sweden N = 31,060 patients who died of heart disease or cancer	Heart disease Cancer	7 days	<p>Symptoms not fully relieved during the last week of life:</p> <ul style="list-style-type: none"> <li>• Dyspnea (10.5% heart disease patients, 6.9% cancer patients)</li> <li>• Confusion (3.9% heart disease patients, 4.4% cancer patients)</li> <li>• Nausea (2.7% heart, 4.1% cancer)</li> <li>• Death rattles (12.9% heart, 12.3% cancer)</li> <li>• Pain (9.8% heart, 14.9% cancer)</li> <li>• Anxiety (12.6% heart, 15.2% cancer)</li> </ul> <p>Patients with heart disease more often (<math>p &lt; 0.001</math>) had dyspnea but cancer patients had significantly more unrelieved symptoms of nausea, anxiety and pain.</p>	
11. Steindal, S.A. et al. (2011) Pain control at the end of life: a comparative study of hospitalized cancer and noncancer patients	Retrospective review of medical records	Norway, hospital N = 220 patients who died	Cancer Heart and vessel disorder Lung diseases Fracture colli femoris Renal failure Other diseases	3 days	<ul style="list-style-type: none"> <li>• Pain (73.5% total sample, 65.5% noncancer patients, 81.7% cancer patients)</li> </ul> <p>Cancer patients had more pain during their last 3 days of life than noncancer patients. The odds of having severe to excruciating pain was more than four times higher for cancer patients compared to noncancer patients.</p>	

Citation	Design and data source	Setting and sample	Diagnoses included	Time frame to death	Symptom prevalence	Prognostic significance of symptoms
12. Elmstedt, S. et al. (2019). Cancer patients hospitalised in the last week of life risk insufficient care quality - a population-based study from the Swedish Register of Palliative Care	Population-based, retrospective study using the Swedish Registry of Palliative Care	Sweden, various settings (hospital, nursing home, palliative care)  N= 41,729 patients with expected cancer deaths	Cancer	7 days	Symptom prevalence reported by place of death. <ul style="list-style-type: none"> <li>Pain (79–85%) and nausea (24–27%) were comparable regardless of setting</li> <li>Other symptoms varied more by setting: anxiety (48%-59%), dyspnea (14%-35%), pulmonary secretions (48%-54%)</li> </ul>	
13. Steindal, S. et al. (2012). Agreement in documentation of symptoms, clinical signs, and treatment at the end of life: a comparison of data retrieved from nurse interviews and electronic patient records using the Resident Assessment Instrument for Palliative Care	Retrospective review of medical records	Norway, hospital N = 112 patients who died	Cancer Heart and vessel disorders Lung diseases	3 days	<ul style="list-style-type: none"> <li>Pain (68%)</li> <li>Dyspnea (73%)</li> <li>Fatigue (89%)</li> <li>Nausea (17%)</li> <li>Difficulty clearing airway secretions (71%)</li> <li>Bloating (3%)</li> <li>Constipation (10%)</li> <li>Diarrhea (8%)</li> <li>Vomiting (17%)</li> <li>Difficulty in falling or staying asleep (26%)</li> <li>Sleep interferes with normal functioning (74%)</li> <li>Dry mouth (19%)</li> <li>Excessive sweating (27%)</li> <li>Peripheral edema (30%)</li> <li>Fever (43%)</li> </ul>	
14. Årestedt, K. et al. (2018). Symptom Relief and Palliative Care during the Last Week of Life among Patients with Heart Failure: A National Register Study.	Population-based, retrospective study using the Swedish Registry of Palliative Care	Sweden, various settings (nursing homes, long-term facilities, hospital wards, specialized palliative care) N = 3,981 patients with expected deaths and heart failure as the underlying cause of death	Heart failure	7 days	<ul style="list-style-type: none"> <li>Pain (62.2%)</li> <li>Rattles/respiratory secretion (51.1%)</li> <li>Anxiety (39.0%)</li> <li>Shortness of breath (29.2%)</li> <li>Confusion (24.9%)</li> <li>Nausea (11.2%)</li> </ul>	

Citation	Design and data source	Setting and sample	Diagnoses included	Time frame to death	Symptom prevalence	Prognostic significance of symptoms
15. Bruijns, S.R.G. et al. (2013). The value of traditional vital signs, shock index, and age-based markers in predicting trauma mortality	Prognostic/epidemiologic study. Retrospective observational study using data from the Trauma Audit and Research Network database.	United Kingdom, trauma hospitals in England and Wales  N = 71,882 patients seen in the emergency department over the period 1996 to 2006  NOTE: Includes patients 16 and older	Not described	2 days (48 hours)		Mortality at 48 hours was significantly associated with age, vital signs, and all other markers ( $p < 0.001$ ). The top five markers according to their positive likelihood ratios are listed below, with their thresholds for 95% specificity. <ul style="list-style-type: none"> <li>Shock index (SI; heart rate/systolic blood pressure) <math>\geq 0.9</math></li> <li>Shock Index x Age (SIA) <math>\geq 55</math></li> <li>Pulse Max Index (PMI; HR/maximum HR) <math>\geq 70\%</math></li> <li>BPAI (systolic blood pressure / age) <math>\leq 1.5</math></li> </ul> Minpulse (MP; maximum HR (220 - age) - HR) $\leq 44$
16. Badawi, O. B. (2012). Readmissions and death after ICU discharge: development and validation of two predictive models	Retrospective, exploratory cohort study	USA, multicenter study of hospital ICUs  N = 704,963 patients who had been in the ICU. Death was experienced by 0.92% of all patients.	ICU type: Cardiac medical Cardiovascular or Cardiothoracic Surgery Medical Mixed Medical-Surgical Neurological Surgical Trauma	2 days (48 hours)		26 variables were retained in the model predicting death within 48 hours of ICU discharge; these included: <ul style="list-style-type: none"> <li>admission characteristics</li> <li>operative diagnosis</li> <li>ICU length of stay</li> <li>ICU ventilation status</li> <li>last day labs</li> <li>last day physiology</li> </ul> The risk of death model had extremely high discrimination reflected in an auROC of 0.92. Ideally this model can be incorporated into an electronic clinical decision support tool.

Citation	Design and data source	Setting and sample	Diagnoses included	Time frame to death	Symptom prevalence	Prognostic significance of symptoms
17. Yu, S. et al. (2014). Comparison of risk prediction scoring systems for ward patients: a retrospective nested case-control study	Retrospective nested case-control study	USA, hospitals  N = 656 cases non-ICU patients admitted to the hospital with a diagnosis of infection	Pneumonia Urinary tract infection Skin or soft tissue infection Other infection Severe sepsis Chronic liver disease Chronic pulmonary disease Chronic renal disease Congestive heart failure Diabetes HIV Cancer	72 hours		At the 0- to 12-hour interval, seven of the eight scores performed similarly and had an AUC of greater than 0.80 (SOFA AUC 0.83, VIEWS 0.81, PIRO 0.87, SCS 0.83, MEDS 0.85, MEWS 0.82, SAPS II 0.83, and APACHE II 0.80). However, at the 12- to 72-hour intervals, only MEDS continued to predict for mortality with excellent discrimination (AUC >0.80). In this subgroup analysis, the clinical decision rule described in Figure 2 performed even better, with a sensitivity of 79% and a specificity of 72% when predicting for mortality. Even after baseline differences between cases and controls were adjusted for, patients who met the clinical decision rule criteria are much more likely to die during hospitalization compared with patients who did not (ORadj 13.3, 95% CI 5.3 to 33.3).
18. Oh, H. et al. (2016) Temporal patterns of change in vital signs and Cardiac Arrest Risk Triage scores over the 48 hours preceding fatal in-hospital cardiac arrest	Retrospective case-control study	Korea, university hospital.  N = 140 ICU patients	Stroke Pneumonia Renal failure Cancer Sepsis Other	48 hours		Initial changes in systolic blood pressure appeared around 18-20 hours prior to cardiac arrest or death. However, the timings of emergent prominent changes in systolic blood pressure differed in these two groups, i.e., 5 hours before cardiac arrest in case group vs. 10 hours before death from other causes. Similar patterns were

Citation	Design and data source	Setting and sample	Diagnoses included	Time frame to death	Symptom prevalence	Prognostic significance of symptoms
						observed for diastolic blood pressure, that is, diastolic blood pressures started to decrease around 18 hours before cardiac arrest or death and then rapidly decreased at around 5-8 hours in the case and control I groups. Detectable changes in heart rates began at 4 hours before cardiac arrest and became more prominent at 2 hours in the case group. In control I group, heart rates began to decrease in a more gradual manner at 10 hours before death and then decreased rapidly from 4 hours.
19. Stevens, V. et al. (2012) The Utility of Acute Physiology and Chronic Health Evaluation II Scores for Prediction of Mortality among Intensive Care Unit (ICU) and Non-ICU Patients with Methicillin-Resistant Staphylococcus aureus Bacteremia	Retrospective cohort; secondary analysis of data	USA, 2 academic medical centers  N = 200 patients with MRSA bacteremia	ICU patients Non-ICU patients	7 days, 48 hours		Acute physiology and chronic health evaluation (APACHE) II was a significant predictor of death at all time points in both ICU and non-ICU patients. Discrimination was high in all models, with c-statistics ranging from 0.72 to 0.84, and was similar between ICU and non-ICU patients at all time points. APACHE II scores significantly improved the prediction of overall and 48-hour mortality compared with age adjustment alone.
20. Martín-Rodríguez, F. et al. (2019). Accuracy of National Early Warning Score 2 (NEWS2) in Prehospital Triage on In-Hospital Early Mortality: A	Longitudinal prospective observational study	Spain, multi-site hospitals  N = 1,288 patients who were attended by Advanced Life Support (ALS) units and	Trauma and injuries by external agents Other types of medical pathology (i.e., cardiovascular,	48 hours		The system with the best predictive capacity was the NEWS2 with an AUC of 0.891 (95% CI, 0.84-0.94), followed by the GAP with an AUC of 0.834 (95% CI, 0.77-0.89). A NEWS2 equal to or greater

Citation	Design and data source	Setting and sample	Diagnoses included	Time frame to death	Symptom prevalence	Prognostic significance of symptoms
Multi-Center Observational Prospective Cohort Study.		transferred to the emergency department (ED), of whom 69 died within 48 hours	neurological, respiratory, digestive, endocrine, infectious, and genitourinary)			than nine points serves to identify patients at high-risk of early mortality in less than 48 hours.

**Table B2: Signs and Symptoms Assessed by Studies (n=14 total articles)**

<b>Sign or Symptom Assessed</b>	<b>Articles Assessing Prevalence</b>
Pain	11
Dyspnea	9
Anxiety	7
Nausea	7
Respiratory secretions /death rattle	5
Confusion	4
Restlessness/Agitation/Delirium	2
Skin problems (ulcers)	2
Constipation	2
Cough	1
Depression	1
Fever	1
Sleep problems/apnea	1
Diarrhea	1
Edema	1
Vomiting	1
Difficulty swallowing	1
Dry mouth	1
Bloating	1
Excessive sweating	1

**Table B3. Summary of Select Studies Examining Signs and Symptoms in the Last Week of Life Excluded from Kehl (n = 6 total articles)**

Citation	Design and data source	Setting and sample	Diagnoses included	Time frame to death	Symptom prevalence	Prognostic significance of symptoms
1. L. S. Wergeland, L.S. et al. (2019) Opioids, Pain Management, and Palliative Care in a Norwegian Nursing Home From 2013 to 2018	5-year longitudinal study; prospective cohort	Norway; nursing home  N = 100 residents who died	Dementia, including Alzheimer's Cardiovascular Stroke Cancer COPD Pneumonia	3 days	<ul style="list-style-type: none"> <li>• Fatigue 84%</li> <li>• Dyspnea 74%</li> <li>• Pain 49%</li> <li>• Depression 40%</li> <li>• Edema 27%</li> </ul>	
2. Verhofstede, R. et al (2017) End-of-Life Care and Quality of Dying in 23 Acute Geriatric Hospital Wards in Flanders, Belgium	Retrospective, cross-sectional descriptive study  NOTE: Employs retrospective recall (nurse and physician within 1 week of death; family/carer 6 weeks after; only nurse/physician data reported)	Belgium, hospital acute geriatric wards  N = 338 deceased patients who had been hospitalized on the geriatric ward for more than 48 hours	Dementia Cancer Organ failure Neurodegenerative disorder Infectious disease	2 days (48 hours)	<ul style="list-style-type: none"> <li>• Shortness of breath 69%</li> <li>• Restlessness 63%</li> <li>• Pain 59%</li> <li>• Anxiety 55%</li> <li>• Discomfort 54%</li> <li>• Gurgling 53%</li> <li>• Difficulty swallowing 54%</li> <li>• Choking 39%</li> </ul>	

Citation	Design and data source	Setting and sample	Diagnoses included	Time frame to death	Symptom prevalence	Prognostic significance of symptoms
3. Meeussen, K.et al. (2012). Older people dying with dementia: a nationwide study	Retrospective mortality study  NOTE: Employs retrospective recall (physician within 1 week of death)	Belgium  N = 1,108 cases	Dementia Cardiovascular disease Malignancies Respiratory disease Disease of the nervous system Stroke Other	7 days	<p>Patients with dementia:</p> <ul style="list-style-type: none"> <li>Lack of appetite 47%</li> <li>Lack of energy 55%</li> <li>Drowsiness 36%</li> <li>Pain 13%</li> <li>Constipation 8%</li> <li>Dry mouth 13%</li> <li>Difficulty breathing 21%</li> </ul> <p>Patients without dementia:</p> <ul style="list-style-type: none"> <li>Lack of appetite 38%</li> <li>Lack of energy 51%</li> <li>Drowsiness 21%</li> <li>Pain 13%</li> <li>Constipation 6%</li> <li>Dry mouth 9%</li> <li>Difficulty breathing 27%</li> </ul> <p>Patients with dementia were twice as likely to be distressed by drowsiness in the last week of life.</p>	
4. Meeussen, K.et al. (2011). End-of-Life Care and Circumstances of Death in Patients Dying As a Result of Cancer in Belgium and the Netherlands: A	Retrospective mortality study  NOTE: Employs retrospective recall (physician within 1 week of death)	Belgium and the Netherlands  N = 422 patients who died of cancer	Cancer	7 days	<ul style="list-style-type: none"> <li>Lack of appetite 59%</li> <li>Lack of energy 73%</li> <li>Drowsiness 29%</li> <li>Pain 23%</li> <li>Constipation 11%</li> <li>Dry mouth 20%</li> <li>Difficulty breathing 25%</li> </ul>	

Citation	Design and data source	Setting and sample	Diagnoses included	Time frame to death	Symptom prevalence	Prognostic significance of symptoms
Retrospective Comparative						
5. Hendriks, S.A. (2015). From admission to death: prevalence and course of pain, agitation, and shortness of breath, and treatment of these symptoms in nursing home residents with dementia	<p>Longitudinal observational study; prospective and retrospective data collection</p> <p>NOTE: Employs retrospective recall for last data point (physician within 2 weeks of death)</p>	<p>Netherlands, nursing homes and residential care facilities</p> <p>N = 372 newly admitted residents who later died</p>	Dementia, including Alzheimer's	7 days	<ul style="list-style-type: none"> <li>• Pain 78%</li> <li>• Shortness of breath 52%</li> <li>• Agitation 35%</li> </ul> <p>Compared with previous time points, in the last week of life:</p> <ul style="list-style-type: none"> <li>• The prevalence of pain increased significantly (from 67%) to 78% (P = .011).</li> <li>• The prevalence of shortness of breath increased substantially and significantly (from 28%) to 52% (P &lt; .001).</li> <li>• The prevalence of agitation decreased significantly (from 58%) to 35% (P &lt; .001)</li> </ul>	
6. Su, A. et al (2018). Beyond Pain: Nurses' Assessment of Patient Suffering, Dignity, and Dying in the Intensive Care Unit	<p>Retrospective data collection through interviews and medical chart abstraction</p> <p>NOTE: Employs retrospective recall (nurses within 3 weeks of death)</p>	<p>USA, 2 large urban hospitals</p> <p>N = 200 patients who died in the medical ICU (MICU), cardiac care unit, or surgical ICU</p>	<p>Respiratory failure</p> <p>Cardiac arrest</p> <p>Other primary cardiac diagnosis</p> <p>Sepsis/septic shock</p> <p>Trauma</p> <p>Cancer</p> <p>Hemorrhage</p> <p>Neurological</p>	7 days	<ul style="list-style-type: none"> <li>• Trouble breathing 44%</li> <li>• Edema 42%</li> <li>• Physical pain 33%</li> <li>• Painful broken skin 23%</li> <li>• Thirst 31%</li> <li>• Hunger 18%</li> </ul>	

Citation	Design and data source	Setting and sample	Diagnoses included	Time frame to death	Symptom prevalence	Prognostic significance of symptoms
			Other Active malignancy Hematologic malignancy COPD Kidney disease Liver disease		<ul style="list-style-type: none"> <li>• Nausea and/or vomiting 9%</li> <li>• Fecal incontinence 29%</li> <li>• Constipation and/or diarrhea 21%</li> <li>• Urinary incontinence 10%</li> <li>• Loss of control of limbs 36%</li> <li>• Fever or chills 16%</li> <li>• Fatigue 31%</li> <li>• Difficulty sleeping 18%</li> </ul>	

## **Appendix C: Neuropathic Pain Literature Review Strategy**

Abt conducted a limited literature review on neuropathic pain in the context of hospice. Using the MEDLINE/PubMed database, we focused on recent literature (published within the last five years) that satisfied the search criteria listed below. Abt also conducted a supplementary search using Google Scholar. Search terms included: *neuropathic pain, nerve pain, neurogenic pain, neuralgia, hospice care, hospice and palliative care nursing, palliative medicine, palliative care, hospice, hospice care*. **Table C1** presented the results of these searched.

### **Search 1:**

(MM "Neuralgia/CI/EP/MO/NU/PC/PX/RH/TH") –

Limiters - Date of Publication: 20140101-20191231; English Language; Human; Publication Type: Meta-Analysis, Systematic Review

Expanders - Apply equivalent subjects

Search modes - Boolean/Phrase

Number of Results: 42

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### **Search 2:**

(MM "Neuralgia/CI/EP/MO/NU/PC/PX/RH/TH") OR AB ("neuropathic pain" OR dysaesthesia OR "neurogenic pain")

Limiters - Date of Publication: 20140101-20191231; English Language; Human; Publication Type: Meta-Analysis, Systematic Review

Expanders - Apply equivalent subjects

Search modes - Boolean/Phrase

Number of Results: 198

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### **Search 4:**

The combination of **Search 2** (above) and **Search 3** (below):

(MH "Hospice Care") OR (MH "Hospice and Palliative Care Nursing") OR (MH "Palliative Medicine") OR (MH "Palliative Care") OR (MH "Hospices")

Limiters - Date of Publication: 20140101-20191231; English Language; Human; Publication Type: Meta-Analysis, Systematic Review

Expanders - Apply equivalent subjects

Search modes - Boolean/Phrase

Number of Results: 408

Number of Results: 2

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### **Search 5:**

((MM "Neuralgia/CI/EP/MO/NU/PC/PX/RH/TH")) AND ((MM "Hospice Care") OR (MM "Hospice and Palliative Care Nursing") OR (MH "Palliative Medicine") OR (MH "Palliative Care") OR (MH Hospices))

Number of Results: 5

**Table C1: Neuropathic Pain Evidence Table**

Study/Citation	Title	Study Design	Conclusion
<p>Askew RL, Cook KF, Keefe FJ, Michaud K, Trence DL, Amtmann D. (2016). A PROMIS Measure of Neuropathic Pain Quality, <i>Value in Health</i>, 19(5), 623-630.</p>	<p>A PROMIS Measure of Neuropathic Pain Quality</p>	<p>A candidate item pool of 42 pain quality descriptors was administered to participants with osteoarthritis, rheumatoid arthritis, diabetic neuropathy, and cancer chemotherapy-induced peripheral neuropathy.</p>	<p>The five-item Patient Reported Outcome Measurement Information System (PROMIS PQ-Neuro) Neuropathic Pain Quality Scale is a short and practical measure that can be used to identify patients more likely to have neuropathic pain and to distinguish levels of NP. The data collected will support future research that targets other unidimensional pain quality domains</p>
<p>N/A</p>	<p>Diagnosis and Classification of Neuropathic Pain</p>		<p>This article elaborates on the criteria for possible, probable, and definite cases of NP:</p> <ol style="list-style-type: none"> <li>1. History of a relevant neurological lesion or disease of the somatosensory nervous system and pain in a plausible neuroanatomical distribution.</li> <li>2. Pain associated with sensory signs in the same plausible neuroanatomical distribution.</li> <li>3. Confirmatory diagnostic tests indicate the presence of a lesion or disease of the somatosensory nervous system explaining the pain.</li> </ol>
<p>Deng, Yunkun &amp; Luo, Lei &amp; Yuhuai, Hu &amp; Fang, Kaiyun &amp; Liu, Jin. (2015). Clinical practice guidelines for the management of neuropathic pain: A systematic review. <i>BMC Anesthesiology</i>. 16. 10.1186/s12871-015-0150-5.</p>	<p>Clinical practice guidelines for the management of neuropathic pain: a systematic review.</p>	<p>The management of neuropathic pain (NP) is challenging despite it being the recent focus of extensive research. A number of clinical practice guidelines (CPGs) for the management of NP have been published worldwide over the past 2 decades. This study aimed to assess the quality of these CPGs.</p>	<p>Despite "scoring poorly on their rigor of development," clinical practice guidelines for neuropathic pain are consistent regarding diagnosis, assessment, and pharmacological management. According to this review, the first-line medications for NP are anticonvulsants pregabalin and gabapentin, low dose TCAs, SSNRIs duloxetine and venlafaxine, and topical lidocaine.</p>

Study/Citation	Title	Study Design	Conclusion
<p>Dosenovic, Sijetlana &amp; Jelcic Kadic, Antonia &amp; Jerić, Milka &amp; Boric, Matija &amp; Markovic, Domagoj &amp; Vucic, Katarina &amp; Puljak, Livia. (2017). Efficacy and Safety Outcome Domains and Outcome Measures in Systematic Reviews of Neuropathic Pain Conditions. <i>The Clinical Journal of Pain</i>. 34. 1. 10.1097/AJP.0000000000000574.</p>	<p>Efficacy and Safety Outcome Domains and Outcome Measures in Systematic Reviews of Neuropathic Pain Conditions</p>	<p>This study analyzed outcome domains and measures used in SRs of randomized controlled trials on efficacy and safety of interventions for NeuP and compared them with the core outcome set (COS) and core outcome measures (COMs) for chronic pain recommended by the Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials (IMMPACT).</p>	<p>According to IMMPACT, the following 6 core outcome domains should be considered when designing chronic pain trials: (1) pain, (2) physical functioning, (3) emotional functioning, (4) participant ratings of improvement and satisfaction with treatment, (5) symptoms and adverse events, and (6) participant disposition.</p>
<p>Finnerup, N. B., Haroutounian, S., Kamerman, P., Baron, R., Bennett, D. L., Bouhassira, D., Cruccu, G., Freeman, R., Hansson, P., Nurmikko, T., Raja, S. N., Rice, A. S., Serra, J., Smith, B. H., Treede, R. D., &amp; Jensen, T. S. (2016). Neuropathic pain: an updated grading system for research and clinical practice. <i>Pain</i>, 157(8), 1599–1606. <a href="https://doi.org/10.1097/j.pain.0000000000000492">https://doi.org/10.1097/j.pain.0000000000000492</a></p>	<p>Neuropathic pain: an updated grading system for research and clinical practice</p>	<p>a revised grading system with an adjusted order, better reflecting clinical practice, improvements in the specifications, and a word of caution that even the “definite” level of neuropathic pain does not always indicate causality</p>	<p>This article elaborates on the criteria for possible, probable, and definite cases of NP</p> <ol style="list-style-type: none"> <li>1. History of a relevant neurological lesion or disease of the somatosensory nervous system and pain in a plausible neuroanatomical distribution.</li> <li>2. Pain associated with sensory signs in the same plausible neuroanatomical distribution.</li> <li>3. Confirmatory diagnostic tests indicate the presence of a lesion or disease of the somatosensory nervous system explaining the pain.</li> </ol>
<p>Harada, S., Tamura, F., &amp; Ota, S. (2016). The Prevalence of Neuropathic Pain in Terminally Ill Patients With Cancer Admitted to a Palliative Care Unit: A Prospective Observational Study. <i>American Journal of Hospice and Palliative Medicine</i>, 33(6), 594–598. <a href="https://doi.org/10.1177/1049909115577353">https://doi.org/10.1177/1049909115577353</a></p>	<p>The Prevalence of Neuropathic Pain in Terminally Ill Patients With Cancer Admitted to a Palliative Care Unit: A Prospective Observational Study.</p>	<p>The primary aim of this study was to determine the prevalence of neuropathic pain (NP) in patients with cancer receiving palliative care.</p>	<p>The prevalence of NP in terminally ill patients with cancer in Japanese palliative care units was 18.6%.</p>

Study/Citation	Title	Study Design	Conclusion
<p>Mathieson, Stephanie &amp; Maher, Chris &amp; Terwee, Caroline &amp; de Campos, Tarcisio &amp; Lin, Chung-Wei. (2015). Neuropathic pain screening questionnaires have limited measurement properties. A systematic review. <i>Journal of Clinical Epidemiology</i>. 68. 10.1016/j.jclinepi.2015.03.010.</p>	<p>Neuropathic pain screening questionnaires have limited measurement properties: A systematic review</p>	<p>Online database searches were conducted and two independent reviewers screened studies and extracted data. Methodological quality of included studies and the measurement properties were assessed against established criteria. A modified Grading of Recommendations Assessment, Development and Evaluation approach was used to summarize the level of evidence.</p>	<p>Overall, the DN4 and Neuropathic Pain Questionnaire were most suitable for clinical use. These screening questionnaires should not replace a thorough clinical assessment.</p>
<p>Mehta, Poonam &amp; Claydon, Leica &amp; Hendrick, Paul &amp; Cook, Chad &amp; Baxter, G D. (2015). Pain and Physical Functioning in Neuropathic Pain: A Systematic Review of Psychometric Properties of Various Outcome Measures. <i>Pain Practice</i>. 16. 10.1111/papr.12293.</p>	<p>Pain and Physical Functioning in Neuropathic Pain: A Systematic Review of Psychometric Properties of Various Outcome Measures.</p>	<p>The aim of this systematic review was to evaluate the methodological quality [Consensus-based Standards for the selection of health status Measurement Instruments (COSMIN) guidelines] of studies that evaluated psychometric properties of pain and physical functioning outcome measures used for NeP.</p>	<p>There are 61 unique outcome measures identified to assess pain and physical functioning outcome domains in trials of neuropathic pain, of which many have "fair or poor" methodological quality.</p>
<p>Mu, A., Weinberg, E., Moulin, D. E., &amp; Clarke, H. (2017). Pharmacologic management of chronic neuropathic pain: Review of the Canadian Pain Society consensus statement. <i>Canadian family physician Medecin de famille canadien</i>, 63(11), 844–852.</p>	<p>Pharmacologic management of chronic neuropathic pain: Review of the Canadian Pain Society consensus statement.</p>	<p>A multidisciplinary interest group within the CPS conducted a systematic review of the literature on the current treatments of neuropathic pain in drafting the revised consensus statement.</p>	<p>Many pharmacologic analgesics exist for the treatment of neuropathic pain. Through evidence-based recommendations, the CPS revised consensus statement helps guide family physicians in the management of patients with neuropathic pain.</p>

Study/Citation	Title	Study Design	Conclusion
<p>Mulla, S. M., Buckley, D. N., Moulin, D. E., Couban, R., Izhar, Z., Agarwal, A., Panju, A., Wang, L., Kallyth, S. M., Turan, A., Montori, V. M., Sessler, D. I., Thabane, L., Guyatt, G. H., &amp; Busse, J. W. (2014). Management of chronic neuropathic pain: a protocol for a multiple treatment comparison meta-analysis of randomised controlled trials. <i>BMJ open</i>, 4(11), e006112. <a href="https://doi.org/10.1136/bmjopen-2014-006112">https://doi.org/10.1136/bmjopen-2014-006112</a></p>	<p>Management of chronic neuropathic pain: a protocol for a multiple treatment comparison meta-analysis of randomised controlled trials.</p>	<p>A systematic review of all randomised controlled trials evaluating therapies for chronic neuropathic pain.</p>	<p>N/A</p>
<p>M R Mulvey, E G Boland, D Bouhassira, R Freynhagen, J Hardy, M J Hjermstad, S Mercadante, C Pérez, M I Bennett, Neuropathic pain in cancer: systematic review, performance of screening tools and analysis of symptom profiles, <i>BJA: British Journal of Anaesthesia</i>, Volume 119, Issue 4, October 2017, Pages 765–774, <a href="https://doi.org/10.1093/bja/aex175">https://doi.org/10.1093/bja/aex175</a></p>	<p>Neuropathic pain in cancer: systematic review, performance of screening tools and analysis of symptom profiles.</p>	<p>Systematic literature search identified studies reporting use of Leeds Assessment of Neuropathic Symptoms and Signs (LANSS), Douleur Neuropathique en 4 (DN4) or painDETECT (PDQ) in cancer patients with a clinical diagnosis of neuropathic or not neuropathic pain. Individual patient data were requested to examine descriptor item profiles.</p>	<p>We identified concordance between the clinician diagnosis and screening tool outcomes for LANSS, DN4 and PDQ in patients with cancer pain. Shortcomings in relation to standardized clinician assessment are likely to account for variation in screening tool sensitivity, which should include the use of the neuropathic pain grading system. Further research is needed to standardize and improve clinical assessment in patients with cancer pain. Until the standardization of clinical diagnosis for neuropathic cancer pain has been validated, screening tools offer a practical approach to identify potential cases of neuropathic cancer pain.</p>

Study/Citation	Title	Study Design	Conclusion
<p>Anna Roberto, Silvia Deandrea, Maria Teresa Greco, Oscar Corli, Eva Negri, Massimo Pizzuto, Fabrizio Ruggeri, Prevalence of Neuropathic Pain in Cancer Patients: Pooled Estimates From a Systematic Review of Published Literature and Results From a Survey Conducted in 50 Italian Palliative Care Centers, Journal of Pain and Symptom Management, Volume 51, Issue 6, 2016, Pages 1091-1102.e4, ISSN 0885-3924, <a href="https://doi.org/10.1016/j.jpainsymman.2015.12.336">https://doi.org/10.1016/j.jpainsymman.2015.12.336</a>. (<a href="http://www.sciencedirect.com/science/article/pii/S0885392416300082">http://www.sciencedirect.com/science/article/pii/S0885392416300082</a>)</p>	<p>Prevalence of Neuropathic Pain in Cancer Patients: Pooled Estimates From a Systematic Review of Published Literature and Results From a Survey Conducted in 50 Italian Palliative Care Centers.</p>	<p>Using MEDLINE, Embase, and a previous review, we searched for studies published up to 2014 reporting data on NCP prevalence in adult cancer populations. Pooled prevalence rates from observational prospective studies were computed. The association between NCP prevalence and possible predictors was investigated for oncology and palliative settings. Prevalence rates were extracted from a questionnaire answered by 137 physicians working in 50 Italian centers of palliative care. Estimates from studies conducted in palliative settings and from the experts were analyzed separately and eventually pooled with an informative Bayesian random-effect model.</p>	<p>Twenty-nine observational studies were identified. The overall pooled prevalence was 31.2%, with high heterogeneity; similar figures were observed when oncology and palliative settings were individually considered. A slightly higher prevalence of NCP was detected for hospice/inpatients as compared to outpatients, in both settings. The mean NCP prevalence reported by the survey experts was 44.2%; the pooled Bayesian estimate for the palliative setting corresponded to 43.0% (95% CI: 40.0e46.0). The subgroup with the lowest heterogeneity and where the literature and experts' estimates were closest is hospice/inpatients, with a pooled Bayesian prevalence rate of 34.9% (95% CI: 29.9e41.0). Conclusion. The systematic review and the survey suggest that more than one in three patients with cancer pain also experiences NCP.</p>
<p>Sanderson, Christine &amp; Quinn, Stephen &amp; Agar, Meera &amp; Chye, Richard &amp; Clark, Katherine &amp; Doogue, Matt &amp; Fazekas, Belinda &amp; Lee, Jessica &amp; Lovell, Melanie &amp; Rowett, Debra &amp; Spruyt, Odette &amp; Currow, David. (2014). Pharmacovigilance in hospice/palliative care: Net effect of gabapentin for neuropathic pain. BMJ supportive &amp; palliative care. 5. 10.1136/bmjspcare-2014-000699.</p>	<p>Pharmacovigilance in hospice/palliative care: net effect of gabapentin for neuropathic pain</p>	<p>Multisite, prospective, consecutive cohort of 127 patients, 114 of whom had cancer, who started gabapentin for neuropathic pain as part of routine clinical care.</p>	<p>Overall, 42% of people experienced benefit at a level that resulted in continued use at 21 days.</p>

Study/Citation	Title	Study Design	Conclusion
<p>O. van Hecke, Sophie K. Austin, Rafi A. Khan, B. H. Smith, N. Torrance. Neuropathic pain in the general population: A systematic review of epidemiological studies Published in Pain (03043959), April 2014 DOI 10.1016/j.pain.2013.11.013 Pubmed ID 24291734</p>	<p>Neuropathic pain in the general population: A systematic review of epidemiological studies</p>	<p>The main focus was on neuropathic pain prevalence and/or incidence, either as part of a specific neuropathic pain-related condition or as a global entity in the general population.</p>	<p>A best estimate of population prevalence of pain with neuropathic characteristics is likely to lie between 6.9% and 10%.</p>
<p>Bouhassira, D., In Revue Neurologique. January-February 2019 175(1-2):16-25 Language: English. DOI: 10.1016/j.neurol.2018.09.016, Database: ScienceDirect</p>	<p>Neuropathic pain: Definition, assessment and epidemiology</p>	<p>Summarize these recent evolutions that have impacted the way these pain syndromes are conceptualized and managed both in daily practice and in the clinical research setting</p>	<p>Most recent review of scales for pain assessment which suggests that a number of NP scales have acceptable reliability and validity and provide positive screening for NP based on the patient pain experience. Words used to describe NP are similar by patients in different languages.</p>

## Appendix D: Dyspnea Literature Review Results

**Table D1** presents a summary of 40 articles that quantify dyspnea prevalence by condition.

**Table D2** summarizes 14 articles examining the relationship between anxiety and dyspnea.

**Table D3** presents 13 studies exploring patient and caregiver preferences related to dyspnea management.

**Table D4** summarizes 18 articles describing dyspnea measures and inter-rater reliability. Note that individual articles may be present in multiple tables.

**Table D1: Summary of Studies Quantifying Prevalence of Dyspnea by Condition**

Citation	Study design	Setting and Sample	Diagnoses	Prevalence of Dyspnea by Condition
D. S.-P. Gainza-Miranda, Eva Maria;Alonso-Babarro, Alberto;Varela-Cerdeira, María;Prados-Sánchez, Concepción;Vega-Aleman, Guadalupe; Rodríguez-Barrientos, Ricardo; Polentinos-Castro, Elena (2019). Breaking Barriers: Prospective Study of a Cohort of Advanced Chronic Obstructive Pulmonary Disease Patients To Describe Their Survival and End-of-Life Palliative Care Requirements	Prospective observational cohort study of advanced COPD patients referred to a Palliative Home Care Team (PHCT)	Advanced COPD patients (n=60) referred to the PHCT between January 2014 and February 2017	• COPD	<ul style="list-style-type: none"> <li>• grade IV (mMRC): 90%</li> <li>• grade III (mMRC): 10%</li> </ul> (Dyspnea was the main cause for palliative sedation in 83% of patients.)
J. A. Alaba, Enrique; Martins, Catarina; Faria, Bera; Andia, Berta; Canchi, Erika (2019). Care at the end of life in patients with advanced dementia institutionalized	Descriptive study using SM-EOLD, the PAINAD-Sp scale, the CADEOLD, and the SWC-EOLD to determine symptom presence, severity, and satisfaction with care	Residents with advanced dementia (n=126) living in the Txara 1 Center in Spain from January 2014 to December 2017	• Dementia	• 46%
C.-T. H. Ho, Hua-Shui; Li, Chia-Ing; Liu, Chiu-Shong; Lin, Chin-Yu; Lin, Cheng-Chieh; Lin, Wen-Yuan (2012). Certain bio-psychosocial-spiritual problems associated with dyspnea among advanced cancer patients in Taiwan	Retrospective analysis to evaluate the association between dyspnea and other physical, psychosocial, and spiritual problems	Advanced cancer patients (n=687) admitted to the hospice palliative ward in a tertiary hospital in Taiwan from 2002 to 2005	• Cancer	• On admission: 37.8%

Citation	Study design	Setting and Sample	Diagnoses	Prevalence of Dyspnea by Condition
S. d. O. Bandeali, Amanda Roze; Sinnarajah, Aynharan (2019). Comparing the physical, psychological, social, and spiritual needs of patients with non-cancer and cancer diagnoses in a tertiary palliative care setting	Retrospective chart review	Patients with a non-cancer diagnosis admitted to a tertiary palliative care unit between January 2008 and December 2017 (n=108) and matched patients with cancer diagnoses (n=54)	<ul style="list-style-type: none"> <li>• Cancer</li> <li>• non-cancer</li> </ul>	<ul style="list-style-type: none"> <li>• Cancer: 37%</li> <li>• non-cancer: 63%</li> </ul>
D. K. Kavalieratos, Arif H.; Abernethy, Amy P.; Biddle, Andrea K.; Carey, Timothy S.; Dev, Sandesh; Reeve, Bryce B.; Weinberger, Morris (2014). Comparing unmet needs between community-based palliative care patients with heart failure and patients with cancer	Poisson regression using data from the Palliative Care Research Registry (PCRR), a repository of quality improvement data	Patients with HF (n=334) and patients with cancer (n=697) receiving palliative care in community-based organizations	<ul style="list-style-type: none"> <li>• HF</li> <li>• Cancer</li> </ul>	<ul style="list-style-type: none"> <li>• HF: 25%</li> <li>• Cancer: 18%</li> </ul> <p>(Rated as moderately/severely distressful)</p>
S. H. Freeman, John P.; Stolee, Paul; Garcia, John; Smith, Trevor Frise (2015). Correlates and Predictors of Changes in Dyspnea Symptoms Over Time Among Community-Dwelling Palliative Home Care Clients	Anonymized assessments from the interRAI palliative care assessment instrument (interRAI PC); regression analyses described risk and protective factors for dyspnea	Assessment data completed between 2006 and 2011 of adult palliative home care patients (n=6655) in Ontario, Canada	<ul style="list-style-type: none"> <li>• Cancer</li> <li>• non-cancer</li> </ul>	<ul style="list-style-type: none"> <li>• Overall at baseline: 44.9%</li> <li>• Cancer only: 42.2%</li> <li>• Cancer + non-cancer: 43.5%</li> <li>• Unspecified: 53.9%</li> <li>• Non-cancer only: 62.3%</li> </ul>
D. C. S. Currow, Joanna; Davidson, Patricia M.; Newton, Phillip J.; Agar, Meera R.; Abernethy, Amy P. (2010). Do the trajectories of dyspnea differ in prevalence and intensity by diagnosis at the end of life? A consecutive cohort study	Consecutive cohort study of dyspnea in 5 patient clusters: lung cancer, secondary cancer to lung, HF, end-stage pulmonary disease, and no identifiable cardiorespiratory cause	Patients referred to Silver Chain Hospice Care Service from January 2004 to December 2007 (n=5862)	<ul style="list-style-type: none"> <li>• Cancer (lung)</li> <li>• Cancer (secondary to lung)</li> <li>• HF</li> <li>• End-stage pulmonary disease</li> <li>• No identifiable cardiorespiratory cause</li> </ul>	Patients with malignant conditions experience increased prevalence of dyspnea closer to death.

Citation	Study design	Setting and Sample	Diagnoses	Prevalence of Dyspnea by Condition
L. C. E. C. Pinzon, Matthias; Perrar, Klaus Maria; Zepf, Kirsten Isabel; Letzel, Stephan; Weber, Martin (2013). Dying with dementia: symptom burden, quality of care, and place of death	Cross-sectional study using a survey questionnaire	Random sample of persons who died in the period from 25 May to 24 August 2008 in Germany (n=5000)	<ul style="list-style-type: none"> <li>• Dementia</li> <li>• Other</li> </ul>	<ul style="list-style-type: none"> <li>• Dementia: 56.7%</li> <li>• Non-dementia: 62.9%</li> </ul>
S. A. S. Hendriks, Martin; Hertogh, Cees M. P. M.; van der Steen, Jenny T. (2014). Dying with dementia: symptoms, treatment, and quality of life in the last week of life	Linear regression on physician-completed questionnaires associations with QOL	Nursing home residents with dementia (n=330) in the Dutch End of Life in Dementia study (2007-2011)	<ul style="list-style-type: none"> <li>• Dementia</li> </ul>	<ul style="list-style-type: none"> <li>• Overall: 35%</li> <li>• Advanced dementia: 31%</li> <li>• Less advanced: 38%</li> </ul> <p>(Not statistically different)</p>
H. M. Eriksson, Anna; Hjelm, Katarina; Friedrichsen, Maria (2016). End of Life Care for Patients Dying of Stroke: A Comparative Registry Study of Stroke and Cancer	Retrospective comparative registry study using data from a Swedish national quality register for end-of-life care based on WHO's definition of Palliative care	Patients who had died of stroke (n=1626) and patients who had died of cancer (n=1626)	<ul style="list-style-type: none"> <li>• Cancer</li> <li>• Stroke</li> </ul>	<p>During last week of life:</p> <ul style="list-style-type: none"> <li>• Cancer: 23.3%</li> <li>• Stroke: 16.3%</li> </ul>
Z. W. Ahmadi, Nicholas G.; Lundström, Staffan; Janson, Christer; Currow, David C.; Ekström, Magnus (2016). End-of-life care in oxygen-dependent ILD compared with lung cancer: a national population-based study	Nationwide registry-based cohort study	Patients with oxygen-dependent ILD (n=285) and patients with lung cancer (822) who died between January 1, 2011 and October 14, 2013	<ul style="list-style-type: none"> <li>• Cancer (lung)</li> <li>• ILD</li> </ul>	<ul style="list-style-type: none"> <li>• Cancer (lung): 42%</li> <li>• ILD: 75%</li> </ul>
S. A. Mercadante, Federica; Adile, Claudio; Valle, Alessandro; Fusco, Flavio; Ferrera, Patrizia; Caruselli, Amanda; Cartoni, Claudio; Marchetti, Paolo; Bellavia, Giuseppe; Cortegiani, Andrea; Masedu, Francesco; Valenti, Marco; Porzio, Giampiero (2016). Epidemiology and Characteristics of Episodic Breathlessness in Advanced Cancer Patients: An Observational Study	Observational study of the association pattern between breathlessness and clinical comorbidities	Patients with advanced cancer (n=921) admitted to seven different centers, which included oncology, home care, palliative care unit, or hospice settings, during a period of six months (April 2014 to September 2014)	<ul style="list-style-type: none"> <li>• Cancer</li> </ul>	<p>Persistent breathlessness: 29.3%</p> <p>Episodic breathlessness: 70.9%</p>

Citation	Study design	Setting and Sample	Diagnoses	Prevalence of Dyspnea by Condition
S. A. S. Hendriks, Martin; Galindo-Garre, Francisca; Hertogh, Cees M. P. M.; van der Steen, Jenny T. (2015). From admission to death: prevalence and course of pain, agitation, and shortness of breath, and treatment of these symptoms in nursing home residents with dementia	Longitudinal observational study with up to 3.5 years of follow-up	Long-term care facilities (n=28) in the Netherlands; Newly admitted nursing home residents (n=372) in variable stages of dementia	• Dementia	• At end of life: 35%
A. G. Damani, Arunangshu; Salins, Naveen; Muckaden, M.; Deodhar, Jayita (2019). High prevalence of dyspnea in lung cancer: An observational study	Subset analysis of lung cancer patients of a prospective observational study done over 6 months from April to September 2014	Patients at palliative center at hospital in India with advanced lung cancer (n=42)	• Cancer (lung)	About 71.43% of the patients with advanced lung cancer experienced dyspnea
S.-S. R. Loke, Kung-Ming; Huang, Chih-Fang (2011). Impact of combined hospice care on terminal cancer patients	Evaluation of questionnaire responses using statistical analyses	From January to December 2009, terminal cancer patients who accepted consultation from a hospice team for combined hospice care (n=354)	• Cancer	• 52%
L. C. Rowbottom, Stephanie; Zhang, Liying; McDonald, Rachel; Barnes, Elizabeth; Tsao, May; Zaki, Pearl; Chow, Edward (2017). Impact of dyspnea on advanced cancer patients referred to a palliative radiotherapy clinic	A retrospective analysis conducted on a prospectively collected database	Patients (n=1392) that attended a palliative radiotherapy clinic from 1999 to 2002 and 2006 to 2009	• Cancer (advanced)	• Moderate/severe 1999-2002: 26.4% • Moderate/severe 2006-2009: 24.9%
M. O. Süren, İsmail; Kaya, Ziya; Karaman, Serkan; Arici, Semih; Çömlekçi, Mevlüt; Ayan, Murat; Esen, Mehmet; Doğru, Serkan; Şahin, Aynur; Karaman, Tuğba (2014). Initial experience with delivery of palliative care to terminal cancer patients	Descriptive study of the symptoms and needs of terminal cancer patients in a region where formal palliative care is limited	End-stage cancer patients admitted or referred by various departments to the outpatient pain unit in Turkey in 2011 and 2012 (n=107)	• Cancer	• 63.6%
C. W. H. R. Chan, Alison; Richardson, Janet (2013). An investigation of a symptom cluster in Chinese patients with lung cancer receiving radiotherapy	Quantitative longitudinal study involving secondary analysis of data from a RCT	Convenience sample of patients receiving palliative radiotherapy Hong Kong (n=140)	• Cancer (lung)	• T0: 95.7% • T1: 96.3% • T2: 96.9%

Citation	Study design	Setting and Sample	Diagnoses	Prevalence of Dyspnea by Condition
				<ul style="list-style-type: none"> <li>T3: 97.1% (measured using VAS)</li> </ul>
P. W. White, Suzanne; Edmonds, Polly; Gysels, Marjolein; Moxham, John; Seed, Paul; Shipman, Cathy (2011). Palliative care or end-of-life care in advanced chronic obstructive pulmonary disease: a prospective community survey	Cross-sectional interview study using structured questionnaires generated from 44 south London general practices	Patients with COPD (n=163) and at least two of: forced expiratory volume in the first second (FEV(1)) <40% predicted, hospital admissions or acute severe exacerbations with COPD, long-term oxygen therapy, cor pulmonale, use of oral steroids, and being housebound	<ul style="list-style-type: none"> <li>COPD</li> </ul>	<ul style="list-style-type: none"> <li>Patients with shortness of breath most days/every day: 88%</li> </ul>
P. E. Körner, Katja; Hartmannsgruber, Johann; Metz, Michaela; Steigerwald, Sabrina; Flentje, Michael; van Oorschot, Birgitt (2017). Patient-reported symptoms during radiotherapy : Clinically relevant symptom burden in patients treated with palliative and curative intent	Comparative study of symptom burden between palliative and curative-intent radiation oncology patients using ESAS	Cancer patients at the radiation department of a German hospital between July and Sept. 2013 (n=151)	<ul style="list-style-type: none"> <li>Cancer</li> </ul>	<ul style="list-style-type: none"> <li>Curative, T1: 17.8%</li> <li>Palliative, T1: 28.5%</li> <li>Curative, T2: 18.7%</li> <li>Palliative, T2: 28.5%</li> </ul> <p>(T1=first consultation, T2=end of RT)</p>
R. T. Matsunuma, Hazuki; Takeda, Yoshihiro; Watanabe, Satoshi; Waseda, Yuko; Murakami, Shinya; Kawaura, Yukimitsu; Kasahara, Kazuo (2016). Patients with End-stage Interstitial Lung Disease may have More Problems with Dyspnea than End-stage Lung Cancer Patients	Retrospective study comparing dyspnea burden between 2 diagnosis groups	Patients with a diagnosis of ILD (n=23) or LC (n=59) who were admitted to and died in one hospital in Japan from January 2007 to September 2013	<ul style="list-style-type: none"> <li>Lung disease</li> <li>Cancer (lung)</li> </ul>	<ul style="list-style-type: none"> <li>ILD, 7 days to death: 83%</li> <li>Cancer, 7 days to death: 57%</li> <li>ILD, 3 days to death: 89%</li> <li>Cancer, 3 days to death: 64%</li> <li>ILD, 1 day to death: 91%</li> <li>Cancer, 1 day to death: 56%</li> </ul>
M. L. P. Saphire, Elizabeth H.; Canavan, Maureen E.; Wang, Shi-Yi J.; Presley, Carolyn J.; Davidoff, Amy J. (2020). Patterns of Symptom Management Medication Receipt at End-of-Life Among Medicare Beneficiaries With Lung Cancer	Retrospective cohort study using the Surveillance, Epidemiology, and End Results-Medicare database	Decedents diagnosed with lung cancer at age 67 years and older between January 2008 and December 2013 who survived six months and greater after diagnosis (n=16,246)	<ul style="list-style-type: none"> <li>Cancer (lung)</li> </ul>	<ul style="list-style-type: none"> <li>Received medication for dyspnea: 70.7%</li> <li>Some differences by sex, age, and race/ethnicity</li> </ul>

Citation	Study design	Setting and Sample	Diagnoses	Prevalence of Dyspnea by Condition
D. d. G. Zweers, Everlien; de Graeff, Alexander; Stellato, Rebecca K.; Witteveen, Petronella O.; Teunissen, Saskia C. C. M. (2018). The predictive value of symptoms for anxiety in hospice inpatients with advanced cancer	Retrospective cross-sectional study	Advanced cancer patients admitted to a hospice in the Netherlands from June 2007 - Sept. 2015 (n=211)	• Cancer (advanced)	<ul style="list-style-type: none"> <li>• USD-score 1+: 41%</li> <li>• USD-score&gt;3: 25%</li> </ul>
C. T. Schindera, Deborah; Bartels, Ute; Gillmeister, Biljana; Alli, Amanda; Sung, Lillian (2014). Predictors of symptoms and site of death in pediatric palliative patients with cancer at end of life	Retrospective descriptive study	Pediatric palliative patients with cancer (n=61)	• Cancer	<ul style="list-style-type: none"> <li>• 4 weeks prior to death: 25% any, 10% mild (1-2, CTCAE), 15% (severe 3-5)</li> <li>• Patients with leukemia or receiving IV chemo were more likely to have dyspnea</li> </ul>
A. G. Damani, Arunangshu; Salins, Naveen; Deodhar, Jayita; Muckaden, MaryAnn (2018). Prevalence and Intensity of Dyspnea in Advanced Cancer and its Impact on Quality of Life	Prospective observational cross-sectional study done over a period of 6 months from April to September 2014	Patients with advanced cancer (n=498) at a palliative medicine department in India	• Cancer (advanced)	<ul style="list-style-type: none"> <li>• Baseline: 26.9% mild symptoms (ESAS 1-3)</li> <li>• Baseline: 10.4% moderate symptoms (ESAS 4-6)</li> <li>• Baseline: 5% severe symptoms (ESAS 7-10)</li> <li>• Overall about 44.37% (CDS score)</li> </ul>
L. G. L. J. Soares, André M.; Gomes, Lúcia C.; Pereira, Rogéria; Peçanha, Carla; Goldgaber, Tatiana (2018). Prevalence and intensity of dyspnea, pain, and agitation among people dying with late stage dementia compared with people dying with advanced cancer: a single-center preliminary study in Brazil	Retrospective analysis, involving review of the electronic charts for the Edmonton Symptom Assessment System (ESAS) scores, from death backwards in time (3 days)	Patients who died with dementia (n=57) or cancer (n=54) in a post-acute care facility in Brazil	<ul style="list-style-type: none"> <li>• Dementia</li> <li>• Cancer (advanced)</li> </ul>	<ul style="list-style-type: none"> <li>• Dementia: 60%</li> <li>• Cancer: 72%</li> <li>(3 days prior to death: statistically similar between the two groups)</li> </ul>
M. N. H. Verkissen, Marianne J.; Van Belle, Simon; Kaasa, Stein; Deliens, Luc; Pardon, Koen (2019). Quality of life and symptom intensity over time in people with cancer receiving palliative care: Results from the international European Palliative Care Cancer Symptom study	Longitudinal study with monthly assessments, using the EORTC QLQ-C15-PAL	Patients (n=1739) from 30 palliative care center in 12 countries	• Cancer	<ul style="list-style-type: none"> <li>• 24.5% (6+ months to death)</li> <li>• 27.1% (5-3 months)</li> <li>• 33.7% (2-0 months)</li> <li>(Based on patient-CRF)</li> </ul>

Citation	Study design	Setting and Sample	Diagnoses	Prevalence of Dyspnea by Condition
J. F. Cui, Fang; Shen, Fengping; Song, Lijuan; Zhou, Lingjun; Ma, Xiuqiang; Zhao, Jijun (2014). Quality of life in patients with advanced cancer at the end of life as measured by the McGill quality of life questionnaire: a survey in China	Cross-sectional survey	Patients (n=531) with advanced cancer in 13 hospitals in China	• Cancer	• 19.2% (based on MQOL-Chinese)
H. A. Kawashima, Takashi; Yamagishi, Tetsuro; Ogose, Akira; Ikoma, Miho; Hotta, Tetsuo; Endo, Naoto (2019). Symptom Burden and End-of-Life Palliative Treatments during the Last Two Weeks of Life in Patients with Advanced Musculoskeletal Sarcoma	Retrospective study	Consecutive MSS patients (n=46) with locally advanced/metastatic disease, who died in a hospital in Japan	• Cancer	• 78%
N. K. Gough, Jonathan; Ross, Joy R.; Riley, Julia; Judson, Ian (2017). Symptom Burden in Advanced Soft-Tissue Sarcoma	Cross-sectional survey using the patient-reported Memorial Symptom Assessment Scale Short Form (MSAS-SF)	Patients (n=113) in a sarcoma center undergoing first-line palliative chemotherapy (FLC), active surveillance pre- and post-FLC, or palliative care (PC) alone	• Cancer (advanced soft-tissue sarcoma)	• Whole sample: 49% • FLC: 38% • AS pre-FLC: 33% • AS post-FLC: 63% • palliative: 75%
S. E. Alshemmari, Hanan; Samir, Zainab; Sajnani, Kamlesh; Alsirafy, Samy (2010). Symptom burden in hospitalized patients with cancer in Kuwait and the need for palliative care	Cross-sectional observational study	Patients with no cognitive impairment, hospitalized with a cancer diagnosis at an oncology facility in Kuwait (n=45)	• Cancer	• Total sample: 42.2% • Receiving best supportive care: 57.9% • Receiving cancer therapy with palliative intent: 30.8%
N. G. C. Wysham, Christopher E.; Wolf, Steven P.; Kamal, Arif H. (2015). Symptom Burden of Chronic Lung Disease Compared with Lung Cancer at Time of Referral for Palliative Care Consultation	Comparative study of the symptom burden and survival prognosis for lung cancer and lung disease patients using the QDACT tool	Patients with a primary diagnosis of lung cancer (n=152) or lung disease (n=86) referred to palliative care from Oct. 2012 - Sept. 2014	• Lung disease (COPD or PF) • Cancer (lung)	• Lung disease: 55% • Lung cancer: 41%  (Moderate to severe dyspnea was statistically similar between the two groups)
P. C. C. Barata, Alice; Custodio, Maria P.; Alves, Marta; Papoila, Ana L.; António, Barbosa; Lawlor, Peter G. (2016). Symptom clusters and survival in Portuguese patients with advanced cancer	Prospective cohort study using descriptive statistics on patient reported symptom data to identify	Advanced cancer patients referred to a Portuguese hospital's palliative care	• Cancer (advanced)	• 91% (2+ ESAS-r)

Citation	Study design	Setting and Sample	Diagnoses	Prevalence of Dyspnea by Condition
	statistically and clinically relevant symptom clusters	program from Oct. 2012 - May 2015 (n=301)		
E. Z. McKenzie, Liying; Chan, Stephanie; Zaki, Pearl; Razvi, Yasmeen; Tsao, May; Barnes, Elizabeth; Drost, Leah; Yee, Caitlin; Hwang, Matthew; DeAngelis, Carlo; Chow, Edward (2020). Symptom correlates of dyspnea in advanced cancer patients using the Edmonton Symptom Assessment System	A prospective database was collected and analyzed to extract patient demographics and ESAS scores	Patients attending the Rapid Radiotherapy Response Program (RRRP) in Canada, from February 2016 to April 2017 (n= 252)	• Cancer (advanced)	<ul style="list-style-type: none"> <li>• Mild (ESAS 1-3): 20.2%</li> <li>• Moderate (4-6): 14.3%</li> <li>• Severe (7-10): 9.9%</li> </ul>
D. d. S. Hui, Renata; Chisholm, Gary B.; Bruera, Eduardo (2015). Symptom Expression in the Last Seven Days of Life Among Cancer Patients Admitted to Acute Palliative Care Units	Prospective, observational study using daily ESAS symptom scores in last week of life	Patients with cancer in acute palliative care unit in US (n=52) and Brazil (n=151)	• Cancer	<ul style="list-style-type: none"> <li>• 7 days to death: &gt;30%</li> <li>• &gt;1 day to death: &gt;70% (4+ ESAS)</li> </ul>
S.-Y. L. Tai, Chung-Yin; Wu, Chien-Yi; Hsieh, Hui-Ya; Huang, Joh-Jong; Huang, Chia-Tsuan; Chien, Chen-Yu (2016). Symptom severity of patients with advanced cancer in palliative care unit: longitudinal assessments of symptoms improvement	Prospective study using descriptive statistics on patient-reported symptom data	Patients with advanced cancer admitted to palliative care unit of hospital in Taiwan from Oct. 2004 - Dec. 2009 (n=824)	• Cancer	• 47.8% on day 1 of admission (1+ on 0-4 scale)
M. F. Lavdaniti, Evangelos C.; Troxoutsou, Konstantina; Zioga, Efrosini; Mitsi, Dimitroula; Alikari, Victoria; Zyga, Sofia (2018). Symptoms in Advanced Cancer Patients in a Greek Hospital: a Descriptive Study	Descriptive study	Convenience sample of patients with advanced cancer patients (n=123) in general hospital in Greece	• Cancer	<ul style="list-style-type: none"> <li>• 56.1% severe (7+ ESAS)</li> <li>• 62.8% present (2+ ESAS)</li> </ul>
M. A. B. MacKenzie, Harleah G.; Meghani, Salimah H.; Riegel, Barbara (2016). Unique Correlates of Heart Failure and Cancer Caregiver Satisfaction With Hospice Care	Retrospective cohort study of national data collected in 2011 by the National Hospice and Palliative Care Organization using the 61-item Family Evaluation of Hospice Care survey	Family Evaluation of Hospice Care responses of adult heart failure (n=7324) and cancer (n=23,871) caregivers	<ul style="list-style-type: none"> <li>• Cancer</li> <li>• HF</li> </ul>	In both cohorts reported patient anxiety was associated with lower satisfaction odds by caregivers. Reported dyspnea was more prevalent in the HF population, but its correlation with lower satisfaction suggests that hospice agencies may not be prepared to manage dyspnea related to HF.

Citation	Study design	Setting and Sample	Diagnoses	Prevalence of Dyspnea by Condition
<p>B. S. Alt-Epping, Anke E.; Simon, Steffen T.; Altfelder, Nadine; Hotz, Thomas; Lindena, Gabriele; Nauck, Friedemann 2012 What is special about patients with lung cancer and pulmonary metastases in palliative care? Results from a nationwide survey Journal of palliative medicine</p>	<p>Secondary analysis of the nationwide Hospice and Palliative Care Evaluation (HOPE)</p>	<p>Patients from inpatient palliative care units and hospices (n=5487) from 2006 to 2008</p>	<ul style="list-style-type: none"> <li>• Cancer (lung)</li> </ul>	<ul style="list-style-type: none"> <li>• Cancer (lung), admission: 72.2%</li> <li>• Cancer (lung), discharge: 64.5%</li> </ul>
<p>M. J. Ekström, M. J.; Schiöler, L.; Kaasa, S.; Hjermstad, M. J.; Currow, D. C. (2016). Who experiences higher and increasing breathlessness in advanced cancer? The longitudinal EPCCS Study</p>	<p>Prospective, longitudinal European Palliative Care Cancer Symptom (EPCCS) study</p>	<p>Adults with confirmed incurable cancer enrolled in palliative care, with prospective monthly assessments for up to 6 months, withdrawal or death, whichever came first (n=1698 patients, n=12 countries)</p>	<ul style="list-style-type: none"> <li>• Cancer</li> </ul>	<ul style="list-style-type: none"> <li>• Reported breathlessness at some point during study: 65%</li> <li>• Mild breathlessness (NRS 1-3) as max: 28%</li> <li>• Moderate breathlessness (NRS 4-7) as max: 27%</li> <li>• Severe breathlessness (NRS 8-10) as max: 9%</li> <li>• Comorbid COPD was associated with markedly higher breathlessness severity and patients with lung cancer had more breathlessness compared to patients with other cancer types.</li> <li>• 67 % of patients who died had a breathlessness measurement within the last 3 months of life and 36.7 % within the final 30 days</li> </ul>

**Table D2: Summary of Studies Examining the Relationship between Anxiety and Dyspnea**

Citation	Study design	Setting and Sample	Diagnoses	Anxiety and Dyspnea
C.-T. H. Ho, Hua-Shui; Li, Chia-Ing; Liu, Chiu-Shong; Lin, Chin-Yu; Lin, Cheng-Chieh; Lin, Wen-Yuan (2012). Certain bio-psychosocial-spiritual problems associated with dyspnea among advanced cancer patients in Taiwan	Retrospective analysis to evaluate the association between dyspnea and other physical, psychosocial, and spiritual problems	Advanced cancer patients (n=687) admitted to the hospice palliative ward in a tertiary hospital in Taiwan from 2002 to 2005	• Cancer	Subjects with propriety preparation problem, anxiety, and fear of death were more likely to have dyspnea.
S. A. Mercadante, Federica; Adile, Claudio; Valle, Alessandro; Fusco, Flavio; Ferrara, Patrizia; Caruselli, Amanda; Cartoni, Claudio; Marchetti, Paolo; Bellavia, Giuseppe; Cortegiani, Andrea; Masedu, Francesco; Valenti, Marco; Porzio, Giampiero (2016). Epidemiology and Characteristics of Episodic Breathlessness in Advanced Cancer Patients: An Observational Study	Observational study of the association pattern between breathlessness and clinical comorbidities	Patients with advanced cancer (n=921) admitted to seven different centers, which included oncology, home care, palliative care unit, or hospice settings, during a period of six months (April 2014 to September 2014)	• Cancer	Psychological factors often have been reported as a possible cause of episodic breathlessness. However, it is likely that the relationship could be inverse, and episodic breathlessness contributes to the development of anxiety and depression, for its obvious influence on the psychological sphere.
A. G. Damani, Arunangshu; Salins, Naveen; Muckaden, M.; Deodhar, Jayita (2019). High prevalence of dyspnea in lung cancer: An observational study	Subset analysis of lung cancer patients of a prospective observational study done over 6 months from April to September 2014	Patients at palliative center at hospital in India with advanced lung cancer (n= 42)	• Cancer (lung)	Dyspnea was found to be significantly correlated with anxiety.
D. G. M. Bove, J.; Kaldan, G.; Overgaard, D.; Lomborg, K. (2017). Home-based COPD psychoeducation: A qualitative study of the patients' experiences	Nested post-trial qualitative study using semi-structured interviews	Home-living patients with advanced COPD and anxiety (n=20)	• COPD	Patients felt that anxiety was something they had deal with privately. The patients stated that in situations with anxiety, it was all about gaining control of their thoughts. This perception affected both their level of anxiety and dyspnea.
M. Y. Y. P. Qian, John; Thompson, Michelle; Wong, Darren; Le, Brian; Irving, Louis; Smallwood, Natasha (2018). Individualized breathlessness interventions may improve outcomes in patients with advanced COPD	Prospective cohort study	Patients with severe COPD, experiences of refractory breathlessness, and a stable medical condition (n=26)	• COPD	Anxiety and depression were common, being present in 38% and 35% of participants. Patients placed particular value upon the education and reassurance that an episode of

Citation	Study design	Setting and Sample	Diagnoses	Anxiety and Dyspnea
				breathlessness would resolve, thereby limiting associated feelings of panic.
C. W. H. R. Chan, Alison; Richardson, Janet (2013). An investigation of a symptom cluster in Chinese patients with lung cancer receiving radiotherapy	Quantitative longitudinal study involving secondary analysis of data from a RCT	Convenience sample of patients receiving palliative radiotherapy Hong Kong (n=140)	• Cancer (lung)	Anxiety decreased over time from 78.6% at T0 to 64.7% at T3. There was moderate positive intercorrelation between breathlessness, fatigue, and anxiety at T0-3 for patients who had experienced all 3 together.
N. S. Livermore, Louise; McKenzie, David (2010). Panic attacks and panic disorder in chronic obstructive pulmonary disease: a cognitive behavioral perspective	Review of panic disorder in COPD patients		• COPD	Panic disorder can heighten perceptions of ambiguous sensations like dyspnea in COPD patients. Anxiety can exacerbate dyspnea itself through increased respiratory rate and hyperventilation.
S. H. Hofmann, Stephanie; Klein, Carsten; Lindena, Gabriele; Radbruch, Lukas; Ostgathe, Christoph (2017). Patients in palliative care—Development of a predictive model for anxiety using routine data	Development of a predictive model for anxiety using data from the standard documentation routine	Data sets of palliative care patients collected by the German quality management benchmarking system called Hospice and Palliative Care Evaluation (HOPE) from 2007 to 2011		Dyspnea is found to predict anxiety, with an increased predictive power with increased severity.
D. d. G. Zweers, Everlien; de Graeff, Alexander; Stellato, Rebecca K.; Witteveen, Petronella O.; Teunissen, Saskia C. C. M. (2018). The predictive value of symptoms for anxiety in hospice inpatients with advanced cancer	Retrospective cross-sectional study	Advanced cancer patients admitted to a hospice in the Netherlands from June 2007 - Sept. 2015 (n=211)	• Cancer (advanced)	<ul style="list-style-type: none"> <li>• Anxiety was uncommon and rarely severe: 25% had a score of <math>\geq 1</math>; 14% had a score <math>&gt;3</math>.</li> <li>• Dyspnea (<math>p=0.01</math>) was an independent predictors for anxiety and, with pain, explained 23% of the variation in anxiety.</li> </ul>
D. J. A. W. Janssen, Emiel F. M.; Spruit, Martijn A. (2015). Psychosocial consequences of living with breathlessness due to advanced disease	Review of the experience of living with breathlessness with a chronic disease			Breathlessness and anxiety are intertwined: anxiety is an emotional response to breathlessness, but also

Citation	Study design	Setting and Sample	Diagnoses	Anxiety and Dyspnea
				increases the perception of breathlessness.
P. C. C. Barata, Alice; Custodio, Maria P.; Alves, Marta; Papoila, Ana L.; António, Barbosa; Lawlor, Peter G. (2016). Symptom clusters and survival in Portuguese patients with advanced cancer	Prospective cohort study using descriptive statistics on patient reported symptom data to identify statistically and clinically relevant symptom clusters	Advanced cancer patients referred to a Portuguese hospital's palliative care program from Oct. 2012 - May 2015 (n=301)	• Cancer (advanced)	Symptoms were grouped into 3 clusters: the neuro-psycho-metabolic (NPM) cluster included tiredness, lack of appetite, dyspnea, anxiety, and lack of well-being. 43.5% of patients exhibited the NPM cluster.
E. Z. McKenzie, Liying; Chan, Stephanie; Zaki, Pearl; Razvi, Yasmeen; Tsao, May; Barnes, Elizabeth; Drost, Leah; Yee, Caitlin; Hwang, Matthew; DeAngelis, Carlo; Chow, Edward (2020). Symptom correlates of dyspnea in advanced cancer patients using the Edmonton Symptom Assessment System	A prospective database was collected and analyzed to extract patient demographics and ESAS scores	Patients attending the Rapid Radiotherapy Response Program (RRRP) in Canada, from February 2016 to April 2017 (n= 252)		Patients with anxiety have a higher probability of exhibiting moderate/ severe dyspnea.
M. S. Schunk, Friederike; Bausewein, Claudia (2019). What Constitutes Good Health Care for Patients with Breathlessness? Perspectives of Patients, Caregivers, and Health Care Professionals	Multi-perspective qualitative study drawing on semi-structured interviews	Ten patients (COPD n = 3, cancer n = 3, chronic heart failure n = 2, and lung fibrosis n = 2), 3 caregivers, and 10 HCPs	• Cancer • COPD • CHF • Lung fibrosis	Anxiety was also one of two predictive variables for dyspnea presence (ESAS of 1 or greater).
M. J. Ekström, M. J.; Schiöler, L.; Kaasa, S.; Hjermstad, M. J.; Currow, D. C. (2016). Who experiences higher and increasing breathlessness in advanced cancer? The longitudinal EPCCS Study	Prospective, longitudinal European Palliative Care Cancer Symptom (EPCCS) study	Adults with confirmed incurable cancer enrolled in palliative care, with prospective monthly assessments for up to 6 months, withdrawal or death, whichever came first (n=1698 patients, n=12 countries)	• Cancer	The pivotal crisis point mentioned by patients and caregivers is when breathlessness triggers anxiety. A 24/7 telephone hotline and home visits by physicians are identified as services most needed.

**Table D3: Summary of Studies Examining Patient and Caregiver Preferences Related to Dyspnea**

Citation	Study design	Setting and Sample	Diagnoses	Patient and Caregiver Preferences
S. T. N. Simon, Anna Maria; Benalia, Hamid; Voltz, Raymond; Higginson, Irene	Structured face-to-face interviews	Patients suffering from breathlessness from lung cancer	• Cancer • COPD	• Inhaled was the most accepted (87%) and preferred (68%) route of opioid

Citation	Study design	Setting and Sample	Diagnoses	Patient and Caregiver Preferences
J.; Bausewein, Claudia (2012). Acceptability and preferences of six different routes of drug application for acute breathlessness: a comparison study between the United Kingdom and Germany		(LC), chronic obstructive pulmonary disease (COPD), chronic heart failure (CHF), and motor neuron disease (MND) in the UK (n=48), Germany (n=71)	<ul style="list-style-type: none"> <li>• CHF</li> <li>• MND</li> </ul>	<p>application, followed by sublingual (45%/13%) and intranasal (42%/8%). The oral was least accepted (24%) and least preferred (9%) although nearly all participants had previous experiences with it (97%).</p> <ul style="list-style-type: none"> <li>• There were some differences in acceptability and preference between diagnosis groups and country.</li> </ul>
C. H. Dunger, Irene J.; Gysels, Marjolein; Booth, Sara; Simon, Steffen T.; Bausewein, Claudia (2015). Breathlessness and crises in the context of advanced illness: A comparison between COPD and lung cancer patients	Qualitative study embedded in a longitudinal study using topic guided in-depth interviews	Purposive sample of patients with breathlessness affecting their daily activities due to advanced lung cancer (n=8) or COPD (n=10) from three hospitals, two respiratory surgeries, and a palliative home care service in Germany	<ul style="list-style-type: none"> <li>• COPD</li> <li>• Cancer (lung)</li> </ul>	While COPD patients were more likely sought to get their life with breathlessness under control, the participating lung cancer patients often faced the possibility of death and expressed a need for security.
J. W. Ellis, Richard; Tishelman, Carol; Williams, Mari Lloyd; Bailey, Chris D.; Haines, Jemma; Caress, Ann; Lorigan, Paul; Smith, Jaclyn A.; Booton, Richard; Blackhall, Fiona; Molassiotis, Alexander (2012). Considerations in developing and delivering a nonpharmacological intervention for symptom management in lung cancer: the views of patients and informal caregivers	Semi-structured interviews and framework analysis regarding the issues that were perceived to be important concerning a nonpharmacological intervention	Patients with lung cancer (n=37) and caregivers (n=23); they were an average of 16 months post-diagnosis	<ul style="list-style-type: none"> <li>• Cancer (lung)</li> </ul>	Patients were more likely to use interventions that they perceived as relevant to them, beneficial in the short term, convenient to their daily routine, flexible enough to accommodate personal preferences, aligned with their beliefs about health care, well-timed, in an appropriate setting, delivered by an appropriate person.
R. B. Thongkhamcharoen, Katrina; Agar, Meera; Hamzah, Ednin (2012). Dyspnea management in palliative home care: a case series in Malaysia	Observation of the clinical management of dyspnea and audit of the associated medical records undertaken during author's clinical attachment Nov-Dec 2010	Patients receiving care from an organization in Malaysia that provides hospice and palliative care (n=5)	<ul style="list-style-type: none"> <li>• Cancer</li> <li>• IPF</li> <li>•Neurodegenerative disease</li> </ul>	Culture and family preferences can impact the reaction to symptoms and treatment options. Asian culture and the individual autonomy concept needed to be adapted to involve family opinions in advance care planning.

Citation	Study design	Setting and Sample	Diagnoses	Patient and Caregiver Preferences
M. G. Ben Natan, Doron; Shachar, Irit (2010). End-of-life needs as perceived by terminally ill older adult patients, family and staff	Descriptive, cross-sectional study	451 subjects, including terminally ill older adult patients (n=73), family members (n=58), physicians (n=7) and 249 nurses (N=249), from two Israeli geriatric centers		Over 60% of the patients were not interested in using all means to prolong their lives, including artificial feeding and respiration, when there was no potential cure. The five needs identified by participants as most important were: not suffering pain, no difficulty breathing, maintaining dignity, having someone who listens, and adequate nursing care.
M. Y. Y. P. Qian, John; Thompson, Michelle; Wong, Darren; Le, Brian; Irving, Louis; Smallwood, Natasha (2018). Individualized breathlessness interventions may improve outcomes in patients with advanced COPD	Prospective cohort study	Patients with severe COPD, experiences of refractory breathlessness, and a stable medical condition (n=26)	• COPD	Patients reported that the intervention was highly useful and acceptable.
C. S. B. Peng, Kelly; Lally, Kate M. (2019). Music Intervention as a Tool in Improving Patient Experience in Palliative Care	Mixed quantitative and qualitative pilot study	Patients receiving a hospice or palliative care consult at 2 hospitals in the Care New England health-care system (n=46)		In giving patients the ability to make a choice, this approach empowered patients, granting back the important impetus of control that many may have relinquished over the course of disease. Second, a live musician can interact with a patient and modify their music choice based on the patient's wants and needs in a dynamic and intuitive fashion.
L. Z. Khan, Liang; Cella, David; Thavarajah, Nemica; Chen, Emily; Zhang, Liyang; Bennett, Margaret; Peckham, Kenneth; De Costa, Sandra; Beaumont, Jennifer L.; Tsao, May; Danjoux, Cyril; Barnes, Elizabeth; Sahgal, Arjun; Chow, Edward (2012). Patients' and Health Care Providers' Evaluation of Quality of Life Issues in Advanced Cancer Using Functional Assessment of Chronic Illness	Comparative study of the ratings of QOL issues (measured using FACIT-Pal) by patients and HCPs	Patients with advanced cancer (n=60) and health-care professionals (HCPs) involved in their care (n=56) at Sunnybrook Health Sciences Centre, Toronto, Canada	• Cancer (advanced)	There was significant mismatch between the perceived impact of dyspnea on QOL by patients and HCPs. HCPs ranked in the following order: pain (73.2%), lack of energy (63.4%), nausea (51.2%) and dyspnea (51.2%) whereas patients rated dyspnea at 9.09%.

Citation	Study design	Setting and Sample	Diagnoses	Patient and Caregiver Preferences
Therapy - Palliative Care Module (FACIT-Pal) Scale				
D. M. Jaturapatporn, Erica; Obwanga, Chris; Husain, Amna (2010). Patients' experience of oxygen therapy and dyspnea: a qualitative study in home palliative care	Qualitative in-depth interviews using an interview guide	Purposive sample of in-home palliative patients in Canada (n=8)	• Cancer (advanced)	Oxygen improved patients' functional capacity and was perceived as "lifeline" or "life saving". Patients perceived disadvantages as comparatively minor - mobility issues, transport, discomfort in nasal cavity and ears.
S. A. Mercadante, Claudio; Aielli, Federica; Lanzetta, Gaetano; Mistakidou, Kyriaki; Maltoni, Marco; Soares, Luiz Guilherme; De Santis, Stefano; Ferrera, Patrizia; Rosati, Marta; Rossi, Romina; Casuccio, Alessandra (2019). Personalized Goal for Dyspnea and Clinical Response in Advanced Cancer Patients	Secondary analysis of a large international study	Age of 18 years and a diagnosis of advanced cancer were the inclusion criteria; exclusion criteria were no dyspnea, a life expectancy of <14 days, and a significant level of cognitive failure (n=279)	• Cancer (advanced)	Most patients (94.2%) indicated a Personalized Dyspnea Intensity Goal of $\leq 3$ as a target at T0. The mean values of PDIG at T0 and T7 were 0.97 and 0.71. Thus, the PDIG significantly changed after one week (P=0.039).
D. P. Hui, Minjeong; Shamieh, Omar; Paiva, Carlos Eduardo; Perez-Cruz, Pedro Emilio; Muckaden, Mary Ann; Bruera, Eduardo (2016). Personalized symptom goals and response in patients with advanced cancer	Prospective longitudinal multicenter study	Patients (n=728) from 5 tertiary care hospitals		Patients on average felt comfortable with dyspnea at a level of 2 out of 10, with a range of 0 to 6.
D. H. K. Ferreira, Slavica; Honson, Aaron; Phillips, Jane L.; Currow, David C. (2020). Two faces of the same coin: a qualitative study of patients' and carers' coexistence with chronic breathlessness associated with chronic obstructive pulmonary disease (COPD)	Randomised, placebo-controlled effectiveness study (RCT)	Patient and carer pairs (n=9) in South Australia	• COPD	Both patients and carers reported that COPD associated breathlessness took over their lives. While patients experienced breathlessness on a daily basis and had learnt how to accept and adapt to the symptom, carers were frequently distressed by watching patients trying to catch their breath. Episodes of acute breathlessness are more difficult for patients than daily breathlessness.

Citation	Study design	Setting and Sample	Diagnoses	Patient and Caregiver Preferences
				Patients and carers not always aligned on what constitutes over-exertion.
M. S. Schunk, Friederike; Bausewein, Claudia (2019). What Constitutes Good Health Care for Patients with Breathlessness? Perspectives of Patients, Caregivers, and Health Care Professionals	Multi-perspective qualitative study drawing on semi-structured interviews	Ten patients (COPD n = 3, cancer n = 3, chronic heart failure n = 2, and lung fibrosis n = 2), 3 caregivers, and 10 HCPs	<ul style="list-style-type: none"> <li>• Cancer</li> <li>• COPD</li> <li>• CHF</li> <li>• Lung fibrosis</li> </ul>	<ul style="list-style-type: none"> <li>• Positive experiences drew on qualities of the patient-HCP relationship as well as on service coverage and access.</li> <li>• Negative experiences were described as infringements of patients' autonomy and unmet needs in terms of service access, coordination, and symptom relief. Patients and caregivers perceived a lack of problem awareness in HCPs.</li> <li>• Patients and caregivers wished to acquire a range of skills that would enable them to take better control of the symptom.</li> </ul>

**Table D4: Summary of Articles Describing Dyspnea Measures and Inter-Rater Reliability**

Citation	Study design	Setting and Sample	Diagnoses	Quality or Symptom Measures and Inter-rater Reliability
W. H. Rhondali, David; Kim, Sun Hyun; Kilgore, Kelly; Kang, Jung Hun; Nguyen, Linh; Bruera, Eduardo (2012). Association between patient-reported symptoms and nurses' clinical impressions in cancer patients admitted to an acute palliative care unit	Comparison of the results of the ESAS on the day of admission (D1) to the unit and 2 days later (D3) to the NI of each patient's physical and psychological distress on D1 and D3	Consecutive patients with advanced cancer admitted to an acute palliative care unit between April and July 2010 (n=118)	• Cancer	On admission there was a weak correlation between the ESAS item score with the NI score for physical distress ( $r = 0.22$ , $p = 0.02$ ), but no correlation 2 days later.
C. C. B. Reilly, Claudia; Garrod, Rachel; Jolley, Caroline J.; Moxham, John; Higginson, Irene J. (2017). Breathlessness during daily activity: The psychometric properties of the London Chest Activity of Daily Living Scale in patients with advanced disease and refractory breathlessness	Cross-sectional secondary analysis of data from a randomised controlled parallel-group, pragmatic, single-blind fast-track trial (randomised controlled trial) investigating the effectiveness of an integrated palliative and respiratory care service for patients with advanced disease and refractory breathlessness.	Breathless patients with advanced malignant and non-malignant disease.		Psychometric analyses suggest that the London Chest Activities of Daily Living Scale is acceptable, reliable and valid in patients with advanced disease and refractory breathlessness.
P. E. C. E. Perez-Cruz, Cecilia; Bonati, Pilar; Batic, Bogomila; Tupper, Laura; Gonzalez Otaiza, Marcela (2016). Caregivers' accuracy in reporting patients' symptom: A preliminary report	Prospective study	Patients with advanced cancer enrolled in the National Program of Palliative Care at a public Hospital in Chile and their caregivers (n=36 pairs)	• Cancer	There was a positive correlation between patients' and caregivers' assessments of dyspnea. Caregivers were more accurate when their worrying thoughts were higher.
R. G. Persichini, Frédéric; Schmidt, Matthieu; Mayaux, Julien; Demoule, Alexandre; Morélot-Panzini, Capucine; Similowski, Thomas (2015). Diagnostic Accuracy of Respiratory Distress	Prospective study of accuracy of RDOS	Communicating ICU patients (n=220) in a single center, 16-bed ICU at a large university hospital		Observation scales incorporating respiratory and behavioral clinical signs can relate with self-evaluated dyspnea in unselected patients admitted to a medical ICU.

Citation	Study design	Setting and Sample	Diagnoses	Quality or Symptom Measures and Inter-rater Reliability
Observation Scales as Surrogates of Dyspnea Self-report in Intensive Care Unit Patients				
K. D. Reavis, Fatsani (2018). Discriminant Validity Testing of the Respiratory Distress Observation Scale...2018 National Teaching Institute Research Abstracts Presented at the AACN National Teaching Institute in Boston, Massachusetts, May 21-24, 2018	Nonexperimental, descriptive, observational study with concurrent and retrospective review of medical records	Patients with cognitive impairment who were receiving mechanical ventilation in a medical ICU (n=148)		There is a correlation between the RDOS and the CPOT scores ( $\rho = 0.15$ ; $P = .02$ ). There is no significant correlation between the RDOS and RASS scores ( $\rho = -0.02$ ; $P = .76$ ). In addition, the CPOT and the RASS scores are slightly correlated ( $\rho = 0.26$ ; $P < .001$ ).
A. R. d. R. S. P. Margarido Vaz Alves, Paulo Sérgio (2018). Dyspnea in palliative care: nursing records and self assessment of dyspnea	Non-random, purposive sampling technique	Nursing records (n=77) for adults with advanced progressive chronic disease who were capable of self-reporting the intensity of their dyspnea on a NRS, and had complete NR available	• Advanced progressive chronic disease	Nurses diagnosed dyspnea at rest and/or functional dyspnea correctly without using a dyspnea assessment tool.
A. E. M. Singer, Daniella; Teno, Joan M.; Lynn, Joanne; Lunney, June R.; Lorenz, Karl A. (2016). Factors Associated with Family Reports of Pain, Dyspnea, and Depression in the Last Year of Life	Retrospective cohort study	Family respondents of 8254 decedents who died between 1998 and 2012		Proxies may differ in the task of estimating physical and emotional symptoms. Despite these issues, bereaved family reports of patient distress are an indicator of an unmet need that requires investigation and can signal a need for improvement.
M. L. T. Campbell, Thomas N. (2015). Intensity cut-points for the Respiratory Distress Observation Scale	Receiver operating characteristic (ROC) curve analysis on patients stratified by four self-reported levels of respiratory distress: none, mild, moderate, and severe.	Adult inpatients recruited from an urban, tertiary care hospital in the Midwest of the United States (n=136)	• Cancer (lung) • CHF • COP • Pneumonia	RDOS of 0–2 suggests little or no respiratory distress; score $\geq 3$ signifies moderate to severe distress.

Citation	Study design	Setting and Sample	Diagnoses	Quality or Symptom Measures and Inter-rater Reliability
<p>S. T. A. Simon, Nadine; Alt-Epping, Bernd; Bausewein, Claudia; Weingärtner, Vera; Voltz, Raymond; Ostgathe, Christoph; Radbruch, Lukas; Lindena, Gabriele; Nauck, Friedemann (2014). Is breathlessness what the professional says it is? Analysis of patient and professionals' assessments from a German nationwide register</p>	<p>Secondary analysis of a cross-sectional, multi-centre and nationwide register (HOspice and Palliative Care Evaluation (HOPE))</p>	<p>Documented inpatients from hospices and palliative care units from 2006 to 2008 who completed the self-assessed MInimal DOcumentation System (MIDOS) were included (n=2,623)</p>		<p>Presence was correctly evaluated by professionals in 80.9% of cases (sensitivity, 81.8%; specificity, 79.8%). Severity of breathlessness was correctly estimated in 65.7% of cases. LoA was good (<math>\kappa=0.62</math>) for the evaluation of presence of breathlessness and moderate (<math>\kappa=0.5</math>) for the estimation of severity. The proportion of over- or underestimated scores was similar</p>
<p>S. M. K. Dy, Kasey B.; Ast, Katherine; Lupu, Dale; Norton, Sally A.; McMillan, Susan C.; Herr, Keela; Rotella, Joseph D.; Casarett, David J. (2015). Measuring what matters: top-ranked quality indicators for hospice and palliative care from the American Academy of Hospice and Palliative Medicine and Hospice and Palliative Nurses Association</p>	<p>A sequential consensus project that identified candidate indicators mapped to NCP Palliative Care Guidelines domains; the list was narrowed through a modified Delphi rating process by key stakeholders</p>	<p>10 indicators including one in the NCP domain Structure and Process, three in Physical Aspects, one in Psychological and Psychiatric Aspects, one in Spiritual and Existential Aspects, and three in Ethical and Legal Aspects</p>		<p>Dyspnea Screening and Management indicator from AMA-PCPI/NCQA: Percentage of patients with advanced chronic or serious life-threatening illnesses who are screened for dyspnea. For those who are diagnosed with moderate or severe dyspnea, a documented plan of care to manage dyspnea exists. (*For ambulatory physician care - not hospice) Screening for Physical Symptoms indicator using PEACE set: Percentage of seriously ill patients receiving specialty palliative care in an acute hospital setting for more than one day or patients enrolled in hospice for more than seven days who had a screening for physical symptoms (pain, dyspnea, nausea, and constipation) during the admission visit.</p>
<p>J. K. Kako, Masamitsu; Kanno, Yusuke; Ogawa, Asao; Miura, Tomofumi; Matsumoto, Yoshihisa (2018). The Optimal Cutoff Point for Expressing Revised Edmonton Symptom Assessment System Scores as Binary Data Indicating</p>	<p>Retrospective study of ESAS-r data to determine optimal cutoff points for physical symptoms</p>	<p>Patients hospitalized in the palliative care unit of one hospital in Japan between September 1, 2014 and May 31, 2015 (n=205)</p>	<ul style="list-style-type: none"> <li>• Cancer</li> </ul>	<p>The optimal cutoff point for dyspnea is ESAS-r of 4 (with an AUC of 0.83, moderate accuracy).</p>

Citation	Study design	Setting and Sample	Diagnoses	Quality or Symptom Measures and Inter-rater Reliability
the Presence or Absence of Symptoms				
E. K. B. Masel, A. S.; Schur, S.; Maehr, B.; Schrank, B.; Simanek, R.; Preusser, M.; Marosi, C.; Watzke, H. H. (2016). The PERS(2) ON score for systemic assessment of symptomatology in palliative care: a pilot study	Analysis of the feasibility and sensitivity of new PERS2ON score, using assessments at admission, day 7, and discharge	Consecutive patients with advanced cancer, admitted to the Palliative Care Unit at the Medical University of Vienna between March 2014 and July 2014 (n=50)		In comparison to other assessment tools, the PERS <sup>2</sup> ON Score does incorporate the possibility of home care. It was easy to use and patients were able to answer all items at the predefined time points. It can also be used by less specified staff, medical students and Palliative Care Consultation Teams and should not only serve as a score to assess symptom burden but also help to perform a structured anamnesis. Uses 0-10 scale for 7 items (max score of 70)
A. H. G. Kamal, Margaret; Maguire, Jennifer M.; Taylor, Donald; Abernethy, Amy P. (2014). Quality measures for palliative care in patients with cancer: a systematic review	Systematic review of MEDLINE/ PubMed and the gray literature for quality measures relevant to palliative care	284 measures, divided according to 8 NQF domains		NQF domain "physical aspects of care" accounts for 35% of quality measures found; dyspnea is addressed in 26% of measures. The number of quality measures for end-of-life and palliative care has grown significantly; the scope and breadth of these measures remain quite focused on a limited set of symptoms, including pain and dyspnea.
M. L. T. Campbell, Thomas; Walch, Julia (2010). A Respiratory Distress Observation Scale for patients unable to self-report dyspnea	Observational design	Consecutive patients referred for inpatient palliative care consultation and at risk for dyspnea who had one or more of lung cancer, chronic obstructive pulmonary disease (COPD), heart failure, or pneumonia (n=89)	<ul style="list-style-type: none"> <li>• Cancer (lung)</li> <li>• COPD</li> <li>• HF</li> <li>• Pneumonia</li> </ul>	• RDOS was associated with use of oxygen (p<0.01), oxygen saturation (p<0.01) and nearness to death (p<0.01), confirming the validity of using the measure when patients cannot self-report dyspnea.
R. A. C. Mularski, Margaret L.; Asch, Steven M.; Reeve, Bryce B.; Basch, Ethan; Maxwell, Terri L.; Hoverman, J. Russell; Cuny, Joanne; Clauser, Steve B.; Snyder, Claire; Seow, Hsien; Wu, Albert	Review of quality of care measures for dyspnea by compiling quality measures identified in systematic searches and reviews			<ul style="list-style-type: none"> <li>• Systematic reviews identified only three existing quality measurement sets that included quality measures for dyspnea care. The existing dyspnea quality measures reported by retrospective evaluations of care assess only four aspects of care.</li> <li>• Since the 2008 AHRQ Symposium, one dyspnea</li> </ul>

Citation	Study design	Setting and Sample	Diagnoses	Quality or Symptom Measures and Inter-rater Reliability
W.; Dy, Sydney (2010). A review of quality of care evaluation for the palliation of dyspnea				<p>quality measure was submitted through NQF and has been approved for use as part of the American Medical Association, Physician Consortium for Performance Improvement (PCPI) palliative care measure set.</p> <ul style="list-style-type: none"> <li>• There are a number of quality indicators evaluating assessment for critically ill patients.</li> <li>• Instruments for assessment of dyspnea include: 1) intensity ratings: VAS, NRS, Borg; 2) functional assessments: MMRC, SOBQ, Oxygen Cost Diagram; 3) QoL: CRQ0, SGRQ, PFSS, AQ20; 4) Qualitative descriptors.</li> </ul>
D. K. S. Kiely, Michele L.; Mitchell, Susan L. (2012). Scales for the evaluation of end-of-life care in advanced dementia: sensitivity to change	Analysis of the sensitivity of the EOLD scales to detect differences in clinically relevant outcomes using linear mixed-effects models	Convenience sample patients (n=323) from nursing homes (NHs) that had greater than 60 beds and were located within a 60-mile radius of metropolitan Boston	• Dementia	SM-EOLD and SWC-EOLD were found to be sensitive to meaningful clinical changes.
L. H. Birkholz, Tina (2018). Using a Dyspnea Assessment Tool to Improve Care at the End of Life	Pre-experimental study using a pretest/posttest format to determine changes in assessment and treatment after RDOS education was provided	Nurses (n=39) who provide end-of-life care at either a non-profit hospice in the Northeast or a medical/surgical unit of a rural community hospital in the Western United States		<ul style="list-style-type: none"> <li>• Receiving RDOS training didn't improve nurses' ability to assess the patient's overall level of perceived comfort and determine a differential diagnosis.</li> <li>• Nurses' treatment selection was different after receiving RDOS training.</li> <li>• Nurses' ability to assess degrees of dyspnea was somewhat impacted by RDOS at certain severity levels.</li> <li>• 97.4% of participants responded that they strongly agreed or agreed that the RDOS was easy to complete and easy to understand and that they would recommend it as an assessment tool for end-of-life dyspnea.</li> </ul>
Q. Y. Zhuang, Grace Meijuan; Neo, Shirlyn Hui-Shan; Cheung, Yin Bun (2019). Validity, Reliability, and Diagnostic Accuracy of the	Assessment of inter-rater, reliability, divergent	Palliative care patients in a tertiary hospital in Singapore (n=122)	<ul style="list-style-type: none"> <li>• Cancer</li> <li>• Renal failure</li> <li>• HF</li> </ul>	• There was high positive correlation between RDOS and Dyspnea-NRS (r=0.702) and moderate positive correlation between RDOS and Dyspnea-Cat (r=0.677). There was negligible correlation between

Citation	Study design	Setting and Sample	Diagnoses	Quality or Symptom Measures and Inter-rater Reliability
Respiratory Distress Observation Scale for Assessment of Dyspnea in Adult Palliative Care Patients	validity and convergent validity of dyspnea scales		<ul style="list-style-type: none"> <li>• COPD</li> <li>• Other</li> </ul>	<p>RDOS and Pain-NRS (<math>r=0.08</math>; all <math>P &lt; 0.01</math>).</p> <ul style="list-style-type: none"> <li>• The RDOS had clinically significant ability to discriminate patients with moderate to severe dyspnea from none to mild dyspnea with an AUC of 0.874 (0.812e0.936).</li> <li>• There was strong inter-rater reliability of the RDOS between two trained raters (a nurse and a doctor) with an ICC of 0.947 (95% CI 0.919 to 0.976).</li> </ul>

## Appendix E: Social Determinants of Health Literature Summary

**Table E1** summarizes literature that addresses the effects of race, gender, sexual orientation, religion, culture, and geography on hospice care.

**Table E1: Social Determinants of Health and Hospice Care Literature Summary**

Race
<ul style="list-style-type: none"> <li>• Among Medicare beneficiaries who died in 2010, 45.8% of whites used hospice compared to 34% of African Americans, 37% of Hispanics, 28.1% of Asian Americans, and 30.6% of Native North Americans. (Johnson, 2013)</li> <li>• Differences in patterns of care between black and white hospice enrollees persist within the same hospice. (Rizzuto, 2018)</li> <li>• Black patients receive more intensive and higher cost treatments at the end of life including greater rates of hospital admission, Emergency Department (ED) visits, and Intensive Care Unit (ICU) stays, gastrostomies for artificial nutrition, mechanical ventilation, and cardiopulmonary resuscitation. (Rizzuto, 2018)</li> <li>• Blacks are less likely to enroll in hospice compared with non-minorities, despite the growth of hospice across the country during the past decade. (Rizzuto, 2018)</li> <li>• Even after enrolling in hospice, black patients are more likely to disenroll in order to seek curative treatment not covered under hospice care. (Rizzuto, 2018)</li> <li>• In a large, national sample of hospice users, blacks had significantly higher rates of hospital admission, ED visits, and hospice disenrollment at the end of life. Results suggest that these higher rates of hospital utilization and hospice disenrollment by blacks compared with whites are attributable to racial differences within the same hospice rather than systematic differences between hospices in hospital utilization and hospice disenrollment rates. (Rizzuto, 2018)</li> <li>• Black patients are more likely to have a preference for life-sustaining therapies and to hold spiritual beliefs that may conflict with the goals of hospice care than white patients. This preference is often attributed to a general distrust in the healthcare system based on the history of racism in medical research and persistent health disparities. (Rizzuto, 2018)</li> <li>• In a study of chronic kidney disease patients, blacks were less likely than whites to understand hospice or to have had end of life discussions with healthcare providers. In the last year of life, blacks are less likely than whites to visit a primary care doctor, which has been associated with higher hospitalization rates and in-hospital deaths for these patients. Poor interpersonal communication between doctors and their black patients has been proposed as a reason for their lack of trust in the healthcare system. It is possible that improving provider communication and patient understanding of hospice could reduce these disparities (Rizzuto, 2018).</li> <li>• Given that hospice care is primarily provided in a patient's home, the quality of care may be largely dependent on the resources of caregivers and availability of support at or near the home of the patient. Evidence suggests that black hospice patients may have a more difficult time accessing appropriate resources. Specifically, their local pharmacy may be less likely to stock adequate pain medication and they are less likely to receive regular visits by a health aide or other health professional. Black patients may face particularly high barriers to access to certain resources, even when compared to white patients at the same hospice, causing them to resort to the hospital or disenroll from hospice. (Rizzuto, 2018)</li> <li>• Minorities are less likely to be informed about different care options at the end-of-life. Less informed individuals, especially those enrolled in FFS Medicare plans, may be more prone to the influence from medical professionals and supplier-induced demand (Chen &amp; Miller, 2017).</li> </ul>
Gender
<ul style="list-style-type: none"> <li>• Studies examining clients' experiences have indicated that men prefer to rely on their partners for support, whereas women rely on a broader range of support from family, friends (S. Clark et al., 2006), or professional services (Wessels et al., 2010). Also, women, but not men, have reported that their complaints of pain have been discounted by health care professionals.</li> <li>• Men more than women have experienced difficulties in undertaking additional household responsibilities when providing care for relatives with cancer at home (Ussher, Sandoval, Perz, Wong, &amp; Butow, 2013). Other studies have found that based on traditional ideologies, women have been positioned as natural caregivers (Ussher &amp; Sandoval, 2008) by health care providers and family members.</li> <li>• Men are more likely to prefer life-sustaining therapies such as cardiopulmonary resuscitation in the face of serious illnesses, including cancer. Women with cancer are more likely to have do-not-resuscitate orders and more likely to prefer palliative care. (Saeed et al., 2018)</li> <li>• Social norms in many societies worldwide provide women with greater permission to express emotions, report symptoms, and seek social support; to be comfortable is considered a right rather than a sign of weakness, a philosophy that is consistent with the goals of palliative care. (Saeed et al., 2018)</li> </ul>

**Table E1: Social Determinants of Health and Hospice Care Literature Summary**

Sexual Orientation
<ul style="list-style-type: none"> <li>● Sexual and Gender Minorities (SGMs) have been found to experience higher rates of poverty, housing insecurity, food insecurity, and workplace discrimination. (Maingi et al., 2018)</li> <li>● Several studies document high levels of mistrust of the health care system particularly among transgender, HIV-positive, and aging SGM populations. (Maingi et al., 2018)</li> <li>● Challenges for hospice include: higher levels of caregiver strain, lack of culturally competent caregiver support and bereavement groups, provider bias (conscious or unconscious), estrangement from family of origin, lack of inclusion of families of choice in decision making. (Maingi et al., 2018)</li> <li>● Transgender patients in hospice and palliative care settings report concerns about receiving consistent and respectful wound care that exposes the genital area after gender reassignment surgery and are very afraid that there are no legal protections in place that can prevent them from being buried under their birth gender. (Maingi et al., 2018)</li> <li>● LGBT persons are more likely to experience economic insecurity, lack health insurance, experience invisibility, and be victimized and mistreated. This is especially true of older LGBT adults. With recent changes in societal attitudes and some progress in addressing legal concerns, hospice and palliative care organizations now have a unique opportunity to lead the health care community by pioneering culturally sensitive and appropriate methods to better serve this population. (Farmer et al., 2015)</li> <li>● A 2009 national study by Lambda Legal found that discrimination and barriers to care prevalent among LGBT populations included: refusal of care due to sexual orientation, gender identity, or HIV status; care delivered without touching the patient or with the use of excessive precautions; harsh or abusive language; blame for health status; and physical roughness or abuse. (Farmer et al., 2015)</li> <li>● Legal uncertainties and lack of recognition of same-sex couples and families of choice increase the need for end-of-life planning to ensure that a person's wishes are honored and executed and, specifically, to limit the legal power of their families of origin if so desired. (Farmer et al., 2015)</li> <li>● Hospice providers can: 1) acknowledge that reconciliation with families of origin may or may not be welcomed or needed and should be discussed and pursued as per patients' wishes, 2) address the increased risk of mental health problems and unique psychosocial barriers that exist for some SGM patients and ensure that existing quality standards for pain and symptom management are met., and 3) include psychosocial distress, suicide risk, financial planning, and relationship with family of origin and current families of choice when performing screening and intake of SGM patients. (Maingi et al., 2018)</li> </ul>
Religion
<ul style="list-style-type: none"> <li>● Many believe that God is the only one who has control over birth and death, and hence, death should not be fought against with life-extending measures. (Krikorian et al., 2020)</li> <li>● Positive religious coping in patients with advanced cancer is associated with receipt of intensive life-prolonging medical care near death, after correcting for age and race. (Phelps et al., 2009)</li> <li>● Patients with strong religious beliefs were more likely to believe that do-not-resuscitate orders are immoral and that God can heal a patient whose condition is deemed to be medically hopeless. (Phelps et al., 2009)</li> </ul>
Culture
<ul style="list-style-type: none"> <li>● Particularly, in some cultures, there is greater trust and increased willingness to allow family members and others to care for them and participate in decision-making. (Krikorian et al., 2020)</li> <li>● Some cultures withhold information from their dying loved one because they fear that learning of their terminal status and discharge to hospice care will hasten the individual's demise because they will lose hope. (Krikorian et al., 2020)</li> <li>● Some cultures believe strongly that death, like birth, is just a natural part of life's journey, and heroic measures or artificial life support should not interfere with the dying process. (Krikorian et al., 2020)</li> </ul>

## Geography

- There is widespread geographic access to hospice in the United States. The vast majority of the population lives within 30 minutes driving time of a hospice, and the average driving time between where people live and the nearest hospice was only 15 minutes. (Carlson et al., 2010)
- Lower income, lower educational attainment, and a lower percentage of the population who are black are associated with a community being more than 30 minutes from a hospice, independent of population density and even in more urban areas. (Carlson et al., 2010)
- Greater distance from a hospice may: 1) mean that the community is too far to receive services, 2) mean that community members are less likely to serve as volunteers, employees, or board members, which may increase language, trust, and cultural issues that have been found to be barriers to hospice enrollment., 3) impede the diffusion of knowledge and understanding of hospice services within a community, which has been found to encourage hospice use. (Carlson et al., 2010)

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